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MULTIPLE BALLOON KYMOGRAPH RECORDING OF THE COMPARATIVE ACTION OF MORPHINE AND PLACEBOS ON THE MOTILITY OF THE UPPER SMALL INTESTINE IN MAN

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ALTHOUGH there is ample evidence that morphine retards the passage of material through the alimentary tract, the mechanism by which this delay occurs is not clear. Adler, Atkinson, and Ivy found in man that therapeutic doses of morphine diminished propulsive motility while increasing "tone" and nonpropulsive contractions. They suggested that this action upset the co-ordination between adjacent bowel segments which, they felt, must be necessary for effective propulsion. Other workers using the balloon technique, fluoroscopy, and the bolus method have noted a decrease in propulsive contractions, although some of these workers observed that there was initially a temporary increase in peristalsis or propulsive activity (12, 13, 14). Abbott and Pendergrass observed that within 2 minutes after the subcutaneous injection of 1/6 to 1/2 grain of morphine, an abrupt tonic contraction of the duodenum occurred nearly obliterating the lumen for 20 minutes. During this phase small rhythmic waves might be present. Then with a fall in tone, contractions rapidly increased for a brief time. As tone decreased and remained below the control level, contractions diminished and duodenal dilatation was often present up to 3 hours after the injection. Tracing patterns suggesting peristalsis were rarely noted after giving morphine. Huidobro found that morphine both increased as well as decreased tone or the sustained tension of the intestinal wall.

As Ivy (2) and Miller have pointed out, there are a number of reasons for the differences of opinion expressed concerning the intestinal action of morphine. Possibly most important has been the failure to observe the effects of the drug for a sufficiently prolonged period and to compare such observations with the spontaneous changes in motility following placebo administration. The possibility has not always been considered, moreover, that adjacent bowel segments might not respond in a similar manner to the drug, a fact which cannot be determined by the single balloon recording technique. In certain instances, the authors have made no distinction between the types of contractions and have not clarified the time relationship between changes in tone and contractile activity.

The site of action of morphine has been discussed elsewhere (8, 10). In brief, it can be

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said that its action on the intestinal muscle is direct and not from its effect on the central nervous system. The mechanism of this peripheral action is not understood and is said to be complicated by the inhibitory effect of morphine on choline esterase resulting in cholinergic stimulation and by its liberation of epinephrine resulting in adrenergic stimulation.

The purpose of this communication has been to review the evidence for the mode of action of morphine in the light of our own observations which were chiefly concerned with the relative effect of morphine and demerol on the upper small intestine. The action of this latter drug will be reported in detail elsewhere (6). Nine observations have been made in 5 healthy subjects and in 4 patients. Both the patients and healthy subjects were free of gastrointestinal complaints at the time of the experiments. The drug was given subcutaneously in a uniform dosage of 10 milligrams and its effect recorded graphically with the balloons in the duodenum and upper jejunum. The results have been compared to 14 observations following the administration of placebos. Six of the subjects receiving morphine also had a placebo test. One observation in an additional patient has been included to show the motility pattern present during abdominal pain due to an intravenous injection of morphine. The use of the multiple balloon recording technique made it possible to evaluate simultaneously motility in from 2 to 3 adjacent segments of the small bowel. The effect of the drug was noted on propulsive contractions, nonpropulsive contractions, and tone.

METHOD

The method of recording and assessing the motility tracings, the technique of drug and placebo administration, the recording of blood pressure, pulse rates, and respirations and the eliciting of symptoms have been described in other communications (4, 5, 7).

Three subjects were tested with 2 balloons, and 6 subjects with 7 balloons in the upper small intestine. The average duration of the predrug recording of motor activity was 63 minutes with a range of from 45 to 110 minutes. The effect of the drug was followed for an average of 210 minutes with a range of from 75 to 295 minutes. Changes in propulsive contractions were assessed by visual inspection of the graphic records taking into account the frequency and amplitude of contractions. Tone, or the sustained tension of the bowel wall, was determined by measuring with a centimeter ruler the average distance between the resting level of contractions and the baseline of each tracing per 5 minute period. Variations in nonpropulsive contractions could not be expressed in quantitative terms, but their general trend was noted. The data which are to be presented include the motor activity recorded for 45 minutes previous to and not later than 4 hours after the administration of the drug. The placebo tests were carried out in a manner similar to the morphine studies.

RESULTS

Morphine given subcutaneously in a dosage of 10 milligrams was found to have two main effects on the motility of the upper small intestine: (1) a diminution in propulsive and nonpropulsive contractions and (2) intermittent increases in tone or sustained tension of the bowel wall. Alterations in motor activity, typical of the action of the drug, are shown in Figure 1. This subject, whose test is listed as No. 5 in Figure 2, received morphine, 10 milligrams, subcutaneously after a 45 minute control period. The upper 3 tracings represent the graphic records of the motility of the duodenum and upper jejunum. The No. 4 tracing shows the activity in the stomach and was not used in the calculation of the effects of the drug. About 4 minutes after the drug was administered, a "spasm," or temporary increase in tone occurred starting in the duodenum and passing forward along the intestine as shown by the elevations of the baseline in tracings Nos. 3, 2, and 1, respectively. The total spasm lasted about 15 minutes. Coincident with the spasms, propulsive contractions disappeared and nonpropulsive contractions became superimposed on the elevated baseline of the tracings. At the end of the spasm propulsive contractions returned to the control levels and were again diminished 10 minutes later when another spasm occurred. Thereafter, spasms appeared intermittently, at intervals of from 15 to 25 minutes followed each

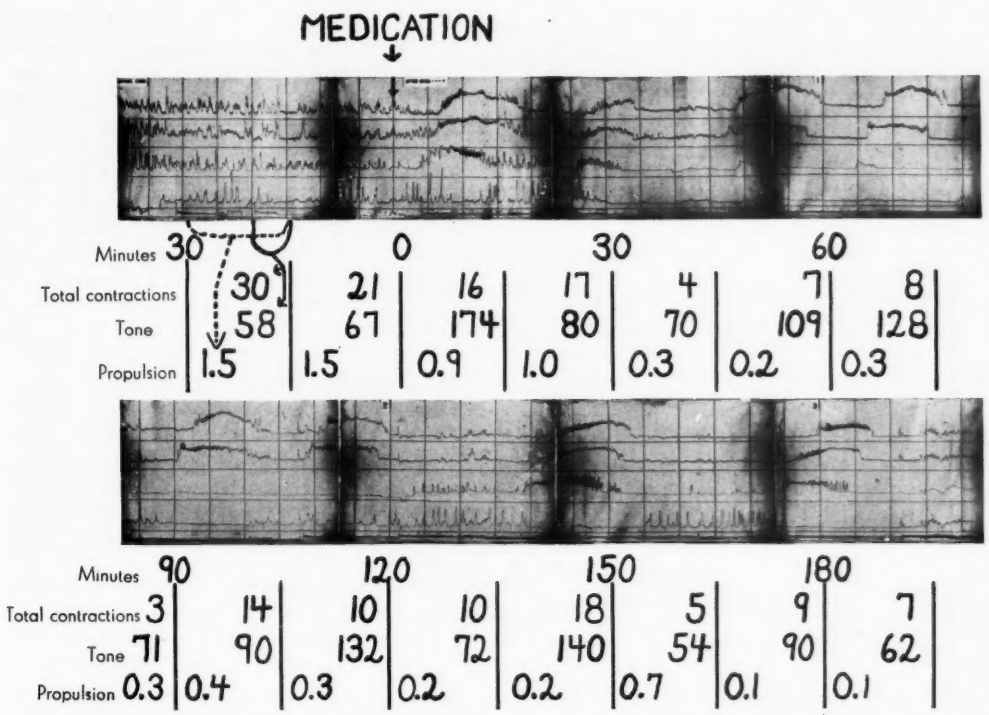

Fig. 1. Upper three tracings show alteration of motility of upper small intestine before and after the subcutaneous injection of 10 milligrams of morphine. The top, or No. 1, tracing was from the upper jejunum, No. 2 tracing from the area near the ligament of Treitz, and the No. 3 tracing from the duodenum. The No. 4 tracing was from the stomach and was not included in the calculation. Time is indicated in intervals of 5 minutes by the vertical lines on the record. The square centimeter area values for total contractions (propulsive and nonpropulsive) and for tone were measured for 5 minutes previous to each 15 minute interval. The propulsion values (arbitrary units) represent the average level of activity for each 15 minute period. Morphine decreased both propulsive and total contractions and caused intermittent spasms over the 200 minute observation period.

time by periods in which propulsive and nonpropulsive contractions were almost completely abolished. During the spasm-free intervals the tone was estimated by measuring the average distance in centimeters between the resting level of contractions and the stationary baseline of the tracings per 5 minute period and was found to be about the same as during the control period. In this subject (No. 5) the tone level, during these spasm-free intervals, varied from +9 to −13 per cent during the 4 hour postdrug recording (Table I). The first 5 minutes and the last 35 minutes of the record have not been included in Figure 1. The square centimeter area values, for total contractions and tone per 5 minute period immediately preceding each 15 minute interval, are shown below the graphic record. The values indicating the changes in propulsive contractions (propulsion) represent the average levels of activity for each 15 minute period. It can be seen that the changes in total contractions (propulsive and nonpropulsive contractions) were similar to those for propulsion. The square centimeter measurements of tone during spasm-free intervals indicated that tone remained slightly elevated except at the 160 to 165 minute and again at the 190 to 195 minute postmedication periods. During spasms tone values were definitely increased.

Propulsive contractions. The decrease in propulsive contractions was much more strik-

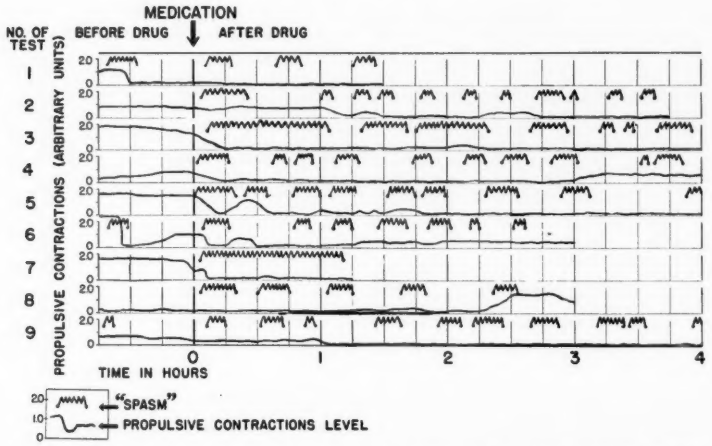

Fig. 2. The graphs show the effect of morphine on upper intestinal motility—the decline in propulsive contractions and the duration and frequency of spasms for each of the 9 tests following the administration of morphine, 10 milligrams subcutaneously. Spasms, or an intermittent, sustained elevation of tone with superimposed nonpropulsive contractions, all occurred within 8 minutes after injection. Within the next 7 minutes there was a maximal decrease in propulsive contractions except for test 2. Tests 1 and 8 were difficult to evaluate because of the minimal propulsive activity before the medication was given.

ing following the administration of morphine (Fig. 2) than in the placebo tests (Fig. 3). Except for tests Nos. 2 and 8, the decrease in contractions was apparent during the first 15 minute interval after morphine was given. In all the tests the initial decline in contractions was associated with the simultaneous occurrence of spasms, which are indicated in Figure 2 by the "saw-toothed" figures. With the exception of test Nos. 4 and 8, the fall-off in propulsive activity was sustained throughout the period of observation. Figure 4 shows the comparison of the percentage decrease in propulsive contractions for the 5 subjects having both the morphine and placebo tests. The subject whose test was indicated as No. 1 in both the placebo and morphine studies (Figs. 2 and 3) was excluded from the determinations in Figure 4 because his propulsive contractions during most of the control period prior to the giving of morphine were minimal. Each test was first compared at intervals of 15 minutes to its average level of propulsive activity for the 45 minutes previous to the administration of the agents. The mean values for each 15 minute interval were then determined by dividing the total values by the number of tests represented in each of the 15 minute periods. Starting with the first quarter-hour postdrug period, at which time there was an 18 per cent decrease in contractions (black arrows), activity was found to decrease progressively until the 60 to 75 minute postdrug interval when the maximal effect of the drug first became apparent. For the remainder of the postdrug period, propulsive contractions were from 81 to 67 per cent less than during the 45 minute control period. As indicated by the white arrows, the decline in propulsive contractions after the placebos were given was much less. The average decrease in propulsive contractions in the placebo tests was 9 per cent with a variation of from +17 to −27 per cent for the 2¾ hours placebo effects were studied.

The variability of the changes in propulsive contraction, typical of that occurring between the 1 and 2¾ hour postdrug periods, is shown by the scattergram at the lower portion of Figure 4. With the placebo tests the percentage change in propulsive activity varied from +40 to −60 per cent. The range of the percentage decline in propulsive contractions, after morphine administration, was from −50 to −100 per cent.

Nonpropulsive contractions. As mentioned elsewhere, changes in nonpropulsive contractions were more difficult to evaluate than variations in propulsive contractions (7). During spasms they frequently appeared to be more marked than during the predrug period. Between spasms they were decreased, as were the propulsive contractions, though the magnitude of such changes could not always be assessed satisfactorily.

Spasms. The frequency and duration of spasms, noted in the morphine tests as compared to the placebo studies, are shown in Figures 2 and 3. In the morphine experiments (Fig. 2), a spasm was found to last anywhere from 8 to 60 minutes and occurred slightly less than once every 15 minutes. In the placebo tests a spasm lasted from 10 to 20 minutes. During the first hour after the giving of the placebos they occurred once in 7 out of the 14 tests. Thereafter, they were present less frequently. In 5 experiments spasms were entirely absent (Fig. 3). In the placebo studies spasms were always associated with a temporary striking decrease in propulsive contractions lasting from about 10 to 105 minutes. It will be noted that in 3 morphine tests and in 1 placebo test spasms occurred before the

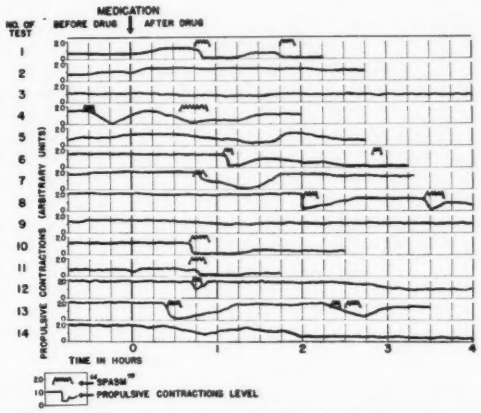

Fig. 3. The figure shows the effect of placebos on upper intestinal motility—the spontaneous changes in propulsive contractions and frequency and duration of spasms noted following the administration of placebos to 12 subjects. The first 6 tests represent the placebo control observations for the morphine studies listed in Figure 2. Each subject having both studies had the same test number.

TABLE I.—SUMMARY DATA OF INDIVIDUAL AND MEAN VALUES SHOWING PERCENTAGE CHANGES IN TONE DURING SPASM-FREE INTERVALS FOR EACH 30 MINUTE PERIOD AFTER THE SUBCUTANEOUS ADMINISTRATION OF 10 MILLIGRAMS OF MORPHINE AND PLACEBOS IN THOSE SUBJECTS HAVING BOTH TESTS*

Subject Number	Agent given	Percentage changes in tone after agents were administered							
		Time in Minutes							
		30	60	90	120	150	180	210	240
1	Morphine	+14	+11	+19	—	—	—	—	—
	Placebo	+16	+28	+31	+28	—	—	—	—
2	Morphine	+27	− 4	+ 7	+ 4	+ 8	+27	+ 4	+ 4
	Placebo	−29	−29	−29	−38	−38	—	—	—
3	Morphine	− 7	+12	−12	−10	−15	−13	−30	−10
	Placebo	−10	− 7	+5	+ 5	+ 7	+ 4	− 3	− 3
4	Morphine	−26	−36	−51	−38	−40	−19	− 3	0
	Placebo	+21	+38	+28	+71	—	—	—	—
5	Morphine	+ 9	+ 2	0	− 6	− 5	−13	− 3	− 7
	Placebo	+ 3	− 5	− 5	− 7	+ 8	—	—	—
6	Morphine	+ 1	− 8	− 4	+ 2	− 7	+ 6	—	—
	Placebo	0	0	0	− 8	−15	−15	—	—
Mean	Morphine	+ 3	− 4	− 7	−10	−12	− 2	− 8	− 3
	Placebo	0	+ 4	+ 5	+ 9	−10	−6	− 3	− 3

*The values for percentage changes in tone were determined by dividing the average value per 30 minute period by the average level for the last 45 minutes of each control period.

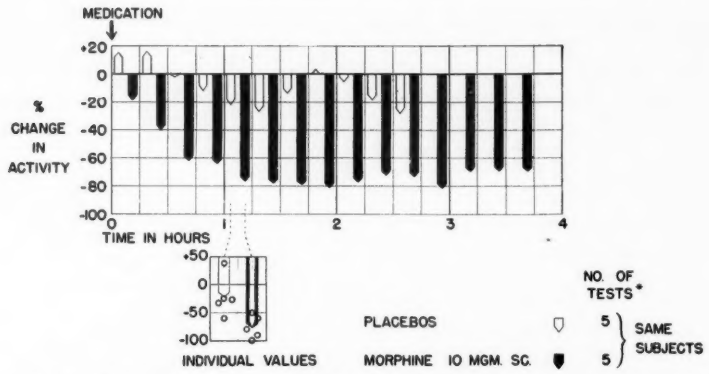

Fig. 4. The chart shows the comparison of the effect of morphine and placebos on propulsive contracts. Predrug and postdrug mean values are compared. The decrease in propulsive contractions was much greater following the subcutaneous administration of 10 milligrams of morphine than after the same subjects received placebos. The mean values for the morphine tests (black arrows) and the placebo tests (white arrows) represent a comparison of the levels of propulsive contractions every 15 minutes as compared to the levels of propulsive activity for the last 45 minutes of the control period. The range of the individual values for the 60 to 75 minute postdrug interval is shown by the scattergram. The variability noted at this time was representative of the extremes of the individual variations noted during the study.

The subjects included in this chart are those numbered 2, 3, 4, 5, and 6 in Figures 2 and 3. The duration of each test can be determined by observing the length of the black lines which indicate the propulsive contraction levels for subject Nos. 2 through 6 in Figures 2 and 3.

medication was given. Their occurrence, prior to the drug administration in these and other studies, made us feel that their presence was not due to the use of the agents per se (3).

As spasms were characterized by an increase in the sustained tension of the bowel wall it was evident that morphine produced striking temporary increases in tone in the intestinal segments studied. Between spasms, however, tone was not appreciably different than during the predrug interval. The individual and mean values for the percentage changes in tone during the spasm-free periods in the subjects having both a morphine and placebo test are shown in Table I. The mean variations in tone in both groups were well within a 12 per cent of the 45 minute control period. The range of the mean values for any half hour interval was from +3 to −12 per cent for the morphine tests and from +9 to −10 per cent for the placebo tests. When the studies were considered individually, the magnitude of variations in tone were found to be about the same in both the morphine and placebo studies. In the morphine studies the tone per 15 minute interval increased as much as 27 per cent in test No. 2 and decreased as much as 51 per cent in test No. 4, whereas in the placebo studies there was a 71 per cent increase in test No. 4 and in test No. 2 a 38 per cent decrease in tone.

Spasms were associated with abdominal complaints in only 1 of the placebo and morphine tests. In the No. 7 morphine test the patient noticed severe epigastric pain during the height of the spasms. That these sustained elevations of tone were capable of giving rise to intestinal pain was further substantiated in another subject receiving intravenous morphine. The subject was a 54 year old female patient, who gave a history of accentuation of epigastric pain when given codeine or morphine for biliary colic. Figure 5 shows that, when she was given 2 to 3 milligrams of morphine intravenously, a pronounced spasm occurred almost immediately in the upper small intestine. At the same time she experienced upper abdominal pain that remained severe during the next 29 minutes as indicated by the arrows. Thereafter, the

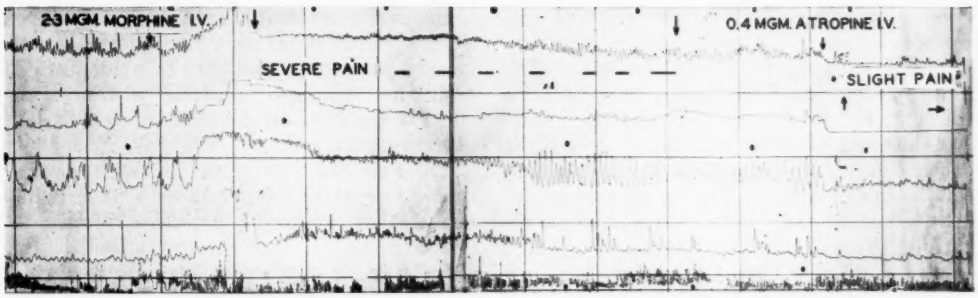

Fig. 5. The graphic record shows spasms occurring in the duodenum and upper jejunum (upper 3 tracings) and also in the stomach (fourth tracing from the top) after the intravenous injection of 2 to 3 milligrams of morphine. Time is indicated at 5 minute intervals by the vertical lines. Severe abdominal pain was present for the period indicated by the 2 top arrows. Atropine, 0.4 milligram, given intravenously, was immediately followed by almost complete relief of pain. This patient gave a history of accentuation of upper abdominal pain, which was presumably biliary tract in origin, whenever she was given codeine or morphine for her attacks.

pain decreased somewhat. After the intravenous injection of atropine, 0.4 milligram, contractions and tone both diminished immediately, leaving patient with only slight abdominal discomfort for about 15 minutes.

Individual variations in response to morphine. As shown in Figure 2, and as mentioned previously, there were only 2 out of 9 tests with morphine in which the decrease in propulsive contractions was not clearly evident within 15 minutes after the giving of the medication. In test No. 2 propulsive contractions did not decrease for 1 hour. The failure of test No. 8 to show a decline in propulsive contractions may have been due to the fact that the contractions were not very pronounced during the 45 minute control period. In both of these tests, however, the drug exerted an immediate effect as evidenced by the occurrence of spasms within 8 minutes following the administration of morphine.

The effect of morphine on individual bowel segments. The use of the multiple balloon recording system permitted a comparison of the effect of morphine on adjacent bowel segments. The action of the drug on propulsive and nonpropulsive contractions, and in producing spasms, was about the same for all the duodenal and jejunal segments studied in a given subject. As shown by the graphic record in Figure 1, spasms always travelled in a forward direction along the intestine. On the other hand, the effect of morphine on tone during the spasm-free periods in adjacent bowel segments was the same in only 3 tests. In 3 other studies 2 segments of bowel showed no change while the third segment showed a slight increase in tone. In the remaining 3 tests the tone change was in a different direction from segment to segment. The differential effect of morphine on tone during the spasm-free intervals did not seem to bear any relationship to the position of the balloons in the duodenum or jejunum.

Side effects of the drug. The incidence of side effects of morphine were minimal in these studies. The association of severe epigastric pain with a sustained increase in tone or spasms in the 1 patient receiving 10 milligrams of the drug subcutaneously, and in the other patient given 2 to 3 milligrams intravenously, has been mentioned. Five subjects reported no side effects. One patient became nauseated for about a half hour period beginning 10 minutes after the drug was injected. Moderate sleepiness was noted in 2. One subject experienced momentary fullness in the head 10 minutes after the injection. No significant changes in blood pressure or heart rate were noted. Respirations were not appreciably affected by morphine.

DISCUSSION AND CONCLUSIONS

The action of morphine on the motility of the upper small intestine has been studied in 9 subjects. The drug was given subcutaneously in a dosage of 10 milligrams. Its effect was compared to the changes in motor activity oc-

curring following the administration of placebos in 14 tests. Six of the subjects receiving morphine were also tested with placebos. The motility was recorded graphically with a multiple balloon water manometer system and the effect of the drug noted on propulsive contractions, nonpropulsive contractions, and tone. On the basis of these observations we have come to the following conclusions regarding the action of the drug:

1. Its initial action occurred from 4 to 8 minutes after the injection of the drug and was characterized by a rather sudden increase in tone as indicated by the spasms, a striking decrease in propulsive contractions and a possible increase in the frequency of nonpropulsive contractions superimposed on the spasms. The temporary initial elevation lasted anywhere from 10 to 60 minutes and was followed by a decrease in tone usually to the predrug levels, for periods varying from 5 to 35 minutes. Thereafter, the cycles of increasing tone and of recovery to the approximate predrug tone levels recurred throughout the remainder of the observation period. After their initial decline, propulsive contractions remained strikingly decreased, although in the transition from elevated tone or spasms to the control levels of tone, propulsive contractions reappeared for short intervals, but not always regularly. Nonpropulsive contractions, which were difficult to evaluate, seemed to remain diminished except during the spasm periods.

2. The maximal effect on propulsive contractions first became apparent at the 60 to 75 minute postdrug period. For the next 90 minutes these contractions were from 67 to 81 per cent decreased as compared to an average decline of 9 per cent in propulsive contractions in the same 5 subjects tested with placebos. For the next hour of observation the decrease in propulsive contractions in the morphine group remained essentially unchanged.

3. The studies were not continued for a sufficiently long period to determine the duration of the action of the drug. The appearance of spasms and the relative absence of propulsive contractions in the 5 tests run for nearly 4 hours indicated that the drug was still active for that period of time. In this connection, it is of interest that Abbott and Pendergrass found that after their human subjects received a therapeutic dose of morphine a normal roentgenographic study could not be made until 24 hours had elapsed. In some instances the effect of the drug on the alimentary tract was detectable for 3 days.

These studies are in agreement with the conclusions of many observers who have maintained that morphine decreases propulsive contractions. If our interpretation of the wave pattern representing propulsive contractions has been correct, we did not find that propulsive waves were at any time increased in relation to the control period when the drug was given subcutaneously, although it was possible that the patient receiving morphine intravenously did show an increase in propulsive contractions in the duodenum (the third tracing from the top in Fig. 5) and that in subject No. 5 propulsive contractions were of a greater magnitude during the 18 to 24 minute postdrug interval as compared to the control period (Fig. 1). Some individuals showed intermittent decreases in tone in all adjacent bowel segments. In others, tone was increased in one segment while decreased in other segments during the absence of spasms. All of the subjects, however, showed intermittent elevations of tone which have been referred to as spasms. The fact that morphine produced intermittent spasms almost simultaneously in all the segments of the small intestine studied, and tended in certain individuals to cause opposite effects on tone in adjacent bowel segments during spasm-free periods, may explain the uneven distribution of barium in the small intestine noted by Abbott and Pendergrass following morphine administration. The failure of certain workers to observe these alternating periods of increased and unchanged tone must have been due, as Miller suggested, to the brief duration of their studies, although Abbott and Pendergrass reported that following a short period of increased motor activity, the relaxation of the duodenum lasted for as long as 3 hours. If it were technically possible to record activity simultaneously over a more extensive area of the intestine, one might determine how far along the gut the spasms travelled. Such a recording technique might also establish whe-

ther or not spasms at any given moment are present in other more widely separated segments of intestine than those studied by us.

Our observations did not permit us to do more than speculate concerning the reason for the delayed transport of intestinal contents following morphine administration. The most obvious explanation, however, is that it is due to the almost complete disappearance of propulsive contractions. The frequent occurrence of spasms must contribute to this delay because of the sustained narrowing of the bowel lumen and the apparent inability of propulsive movements to take place in those segments in which the intestinal muscle cannot relax sufficiently to initiate ample propulsive movements (1, 2).

These studies, following morphine and placebo administration, have made possible adequate control experiments for assessing the action of demerol on the motility of the upper small intestine. In a separate communication it will be reported that the effect of demerol was qualitatively similar to that of morphine but that it produced somewhat less diminution in propulsive contractions and fewer spasms when demerol was injected subcutaneously in dosages of 100 milligrams (6).

SUMMARY

1. The action of the subcutaneous administration of 10 milligrams of morphine on the motility of the upper small intestine has been studied in 9 adult subjects. The findings have been compared to the changes occurring in motility following the administration of placebos to 12 subjects. Six of the subjects receiving morphine were tested with placebos.

2. The action of morphine was characterized by (1) a striking decrease in propulsive contractions and (2) the repeated occurrence of spasms or temporary sudden elevations of tone. During spasm-free periods tone tended to be very slightly decreased after morphine administration. The initial effect of the drug with 2 exceptions occurred within 15 minutes after its injection.

3. It is suggested that, as has already been pointed out by others, morphine retards the transport of material along the alimentary tract due to its action in diminishing propulsive contractions and in causing intermittent spasms.

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EXPERIMENTAL MAINTENANCE OF LIFE BY A MECHANICAL HEART AND LUNG DURING OCCLUSION OF THE VENAE CAVAE FOLLOWED BY SURVIVAL

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THERE is a dual purpose in developing a mechanical apparatus that can perform the functions of the heart and lungs. First, such an apparatus should prove useful in taking over a part of the circulation in patients in whom either the function of the heart or lungs, or both, are impaired to such an extent that life is endangered. Acute coronary thrombosis and acute pulmonary edema exemplify such emergencies, in which temporarily relieving the heart and lungs of a part of the burden of the circulation should allow these organs to recover. To afford such relief, the blood must be rendered incoagulable, venous blood must be continuously withdrawn from one or more peripheral veins and passed through an artificial lung where oxygen is added and carbon dioxide removed. This oxygenated blood must be continuously returned to the body through a needle or a cannula inserted in a central direction in a peripheral artery.

Second, the perfection of such an apparatus should permit operations within the chambers of the human heart under direct vision without a fatal loss of blood. To perform such operations the entire circulation must be taken over temporarily by the mechanical heart and lungs. The requirements are similar to those just listed, but the venae cavae must be clamped at the right auricle and the entire venous return to the heart through these veins must be diverted to the artificial heart and lungs.

The first of these purposes can be more easily achieved than the second. Indeed, it is reasonable to believe that the temporary maintenance of a portion of the circulation by mechanical means in human patients is not far off, because it has already been successfully done in animals by several investigators, including ourselves. Maintaining the entire circulation in human patients will obviously be far more difficult, particularly if an operative procedure is contemplated while the blood is rendered incoagulable.

The efficacy and safety of a mechanical heart and lungs must first be demonstrated by animal experiment. A considerable amount of research has already been carried out along these lines. Many of the techniques which have been used in physiological laboratories for the prolonged perfusion of organs or even whole animals (25, 70) can be applied to the problem. One of us, in 1939, reported the long survival in healthy condition of animals in which all the blood flow through the heart and lungs was completely stopped by clamping the pulmonary artery for as long as 20 minutes, while cardiorespiratory functions were maintained by an extracorporeal circuit (27). This is the first, and to date the only, report of the prolonged healthy survival of animals following perfusion of the whole animal during complete cessation of the blood flow through the heart and lungs.

Because the other organs and tissues of the body can withstand interruption of the circulation longer than the brain (30, 41, 72), several investigators have attempted to keep an animal alive by perfusing the brain alone, while the venae cavae were clamped. O'Shaughnessy in 1939 perfused the brains of animals with a 5 per cent solution of hemoglobin in Ringer's solution during a 10 minute

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period of clamping the venae cavae, and reported the indefinite survival of a 3 kilogram cat and a 7 kilogram dog (56). Bjork (4), working with Crafoord in 1948 perfused the brain of a dog with oxygenated blood while both the venae cavae were clamped for 33 minutes. This animal was observed for 5 months and showed no abnormality in behavior. Perfusion of the brain alone obviously limits the time during which the venae cavae can be clamped, since other organs, for example, the spinal cord and heart, will be damaged by prolonged interruption of the circulation. These latter investigators have now abandoned brain perfusion in favor of perfusion of the whole body (5).

Recently Jongbloed (39) and Dennis have reported the survival of dogs following periods of perfusion of the whole body. Neither of these investigators completely interrupted the flow of blood to the heart by clamping the venae cavae. Jongbloed reported the healthy survival of 1 dog for a year following a 2 hour period of perfusion. The venous blood was withdrawn through 2 catheters, one inserted into the superior vena cava through the external jugular vein, and the other inserted into the inferior vena cava through the femoral vein. The venae cavae were not clamped. It is obvious that the entire circulation of the animal was not carried by the extracorporeal circuit. In 2 other experiments on dogs, each perfused for 2 hours, Jongbloed placed a tightly fitted leather mask over the nose and mouth of each animal for an unstated period of time and found no evidence of anoxemia. He does not report the survival of either of these dogs, and again it is obvious that the test fails to indicate that no blood was passing through the animal's own heart and lungs, and that the entire circulation was being carried by the apparatus (39). Dennis has reported the survival in a healthy condition of several dogs perfused for periods up to 1 hour. In these dogs the right thoracic cavity was opened and venous blood was withdrawn through an opening in the right auricular appendage. In none of these experiments were the venae cavae clamped, so, again, there can be no assurance that the entire circulation was maintained by the extracorporeal circuit.

The basic elements of an extracorporeal blood circuit that will perform the cardiorespiratory functions are two pumps to perform the work of the right and left sides of the heart, and a device which will saturate the blood with oxygen and permit the escape of carbon dioxide. The pumps which have been used by various investigators fall into two categories: those with internal valves and those without. We favor the latter type because an internal valve must necessarily produce some trauma to the cells and turbulence and irregularity in the circuit, factors which tend to promote the formation of fibrin. We have therefore employed a modification of DeBakey's pump (16, 27).

Many methods for the artificial oxygenation of blood have been described. They have been reviewed by Gibbon (26) and Bjork (4). Briefly, three general methods have been used: (a) mechanical mixing of oxygen with blood, by bubbling air (9, 34, 61) or oxygen (12, 33, 54, 65, 74) through venous blood, by injecting oxygen and blood under pressure against the inside of a spherical glass bulb (21), and by administering oxygen intravenously without an attempt at extracorporeal mixing (8, 19, 64, 75); (b) chemical oxygenation by introducing either hydrogen peroxide (50, 55, 63) or sodium percarbonate (47) intravenously; and (c) exposure of blood to oxygen by establishing a blood film on glass beads (6), on a silk curtain (60), over the walls of an inverted bell jar (20, 32), on the walls of concentric cylinders (15, 37), on the wall of a horizontal revolving glass cylinder (24), on the surfaces of a tier of horizontal revolving aluminum plates (3, 22), on vertical rotating plates (4, 45), on a revolving spiral sheet of nickel-plated copper (14), on the inner wall of spiral tubing (38, 39, 46), or by dripping blood through an atmosphere of oxygen (69). None of these methods are thoroughly satisfactory and few workers have successfully oxygenated blood without excessive foaming or destruction of the cellular elements of the blood.

In 1937 Gibbon (26) passed oxygen over a thin film of blood on the inner surface of a revolving vertical cylinder with a surface area of 0.23 square meter. Ninety-eight per cent saturation of the blood could be obtained and ap-

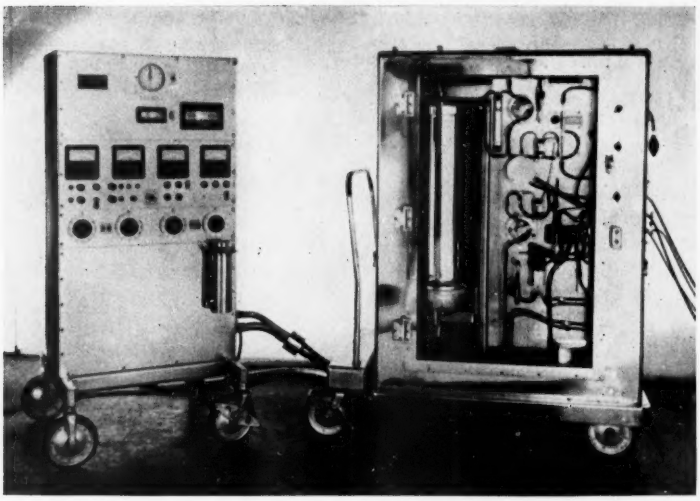

Fig. 1. Photograph of the apparatus. The cabinet on the right with a glass door encloses the extracorporeal circuit in an airconditioned chamber maintained at body temperature. The cabinet at left houses electrical devices which record the operation of, and permit the control of, the blood circuit in the first cabinet.

proximately 18 cubic centimeters of oxygen introduced per minute at a blood flow rate of 534 milliliters per minute. By increasing the surface area of the revolving cylinder to 0.40 square meter, Gibbon introduced 30 cubic centimeters of oxygen per minute at a blood flow rate of 455 milliliters per minute (28).

Bjork (4) in Crafoord's laboratory passed oxygen over a blood film on 50 revolving plates partially immersed in a trough of blood. At any instant the blood film exposed to oxygen was 0.642 square meter. By revolving the plates 2 times per second, 77 square meters of film were exposed per minute, and approximately 131 cubic centimeters of oxygen could be introduced per minute at a flow rate of 800 milliliters of blood per minute. Karlson, Dennis and Westover, in 1949, reported that with multiple horizontal revolving cylinders a maximum of 24.3 cubic centimeters of oxygen per minute could be introduced into the blood. They were unable to oxygenate blood satisfactorily when a thin membrane was interposed between the blood and oxygen, after the principle of Kolff (44). Jongbloed (38) exposed blood to oxygen in a rigid plastic spiral tube, which was revolved about a central axis. Using 6 such tubes he calculates that he is able to introduce as much as 250 cubic centimeters of oxygen per minute (39). Kolff (46) has built and is investigating a modification of this apparatus which requires only 2 pumps and a single revolving drum. He has also modified the Crafoord apparatus (4) to consist of 2 troughs and 2 sets of vertical revolving discs (45). Kolff found foaming difficult to control with both these apparatuses, but both are said to be capable of introducing between 200 and 300 cubic centimeters of oxygen per minute at blood flow rates of 5,000 milliliters per minute (46).

APPARATUS

The apparatus used in these experiments is basically similar to that previously reported (27) and will be described in detail in a later publication (66). The unit consists of two metal cabinets mounted on wheels and connected by a cable inclosing electrical circuits (Fig. 1). The cabinets are small enough to pass through the average sized doorway. The basic parts of the extracorporeal circuit are indicated diagrammatically in Figure 2. Blood is withdrawn from the animal through cannulas in the venae cavae by a roller type (27)

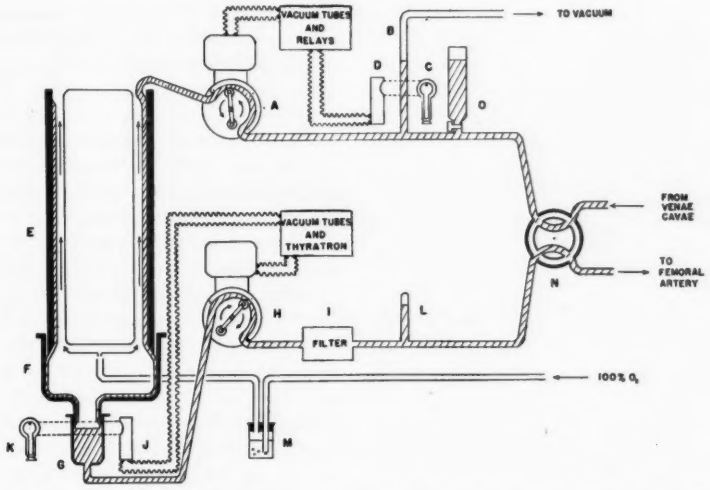

Fig. 2. Diagram of the extracorporeal circuit. For explanations of parts indicated by *A* through *O*, see text.

pump, *A*, hereafter termed the venous pump. If this pump operates too rapidly, the walls of the venae cavae will be drawn into the open ends of the venous cannulae, occluding them. When this occurs the blood level in the vertical tube, *B*, falls, permitting light, *C*, to reach a photoelectric cell, *D*, thus setting into operation an electric circuit which stops the venous pump. The continued intermittent interruption of the venous pump is an indication that its pumping rate should be diminished. The blood from the venous pump flows in a thin film down the inner surface of the vertical revolving cylinder, *E*. During the passage of this film down the inner surface of the cylinder, oxygen enters the blood and carbon dioxide is given off. The blood is collected in a stationary bowl, *F*, and cup, *G*, from which it is pumped by the arterial pump, *H*, through a monel metal filter, *I*, to a cannula directed cephalad in the femoral artery. A constant volume of blood is maintained in the extracorporeal circuit by means of a photoelectric unit consisting of cell, *J*, and light source, *K*. The unit varies the pumping rate of the arterial pump to hold constant a level of blood in the collecting cup, *G*. The closed vertical tube, *L*, eliminates the slight pulsations of the pump, *H*, so there results a smooth nonpulsatile flow into the femoral artery. Oxygen is humidified, *M*, and blown over the blood film in the cylinder, *E*. A quarter turn of the stopcock, *N*, permits a change from recirculation of blood in the apparatus to the perfusion of the animal. The circuit is filled with blood through the burette, *O*.

PREPARATION OF THE APPARATUS

The apparatus was carefully cleaned prior to each perfusion experiment. Since fibrin tended to collect at glass-rubber junctions, these parts were removed and scrubbed separately with an alkaline detergent and rinsed with a large volume of water. All rubber and glass parts were coated internally with silicone, in order to decrease the amount of fibrin deposited in the apparatus during circulation of blood. For 1 hour prior to perfusion sterile water and then sterile saline were recirculated through the apparatus. No antiseptic solutions were used.

Approximately 550 milliliters of blood are required to fill the tubing, collecting cup, and filter, and to lay a film on the inner surface of the cylinder. To avoid depletion of blood volume in the experimental animal, the apparatus was filled with donor blood before each perfusion. Donor dogs were anesthetized with

sodium pentothal (25 mgm. per kgm. of body weight), given heparin (5 mgm. per kgm. of body weight) and under sterile precautions approximately 700 milliliters of blood were withdrawn by femoral artery puncture an hour before the perfusion experiments. The temperature in the air-conditioned cabinet was raised to 37 degrees C. The extracorporeal circuit was then filled with the donor blood, which was recirculated slowly through the apparatus at 200 milliliters per minute. The cylinder was revolved at 50 revolutions per minute and a film of blood established on its inner surface. A mixture of 96 per cent oxygen and 4 per cent carbon dioxide was blown over the blood film at 5 liters per minute. When the circuit was connected to the animal the gas mixture was changed to 100 per cent oxygen. The tubing by which the extracorporeal circuit was to be connected with the animal was filled with blood, and care was taken to eliminate air bubbles.

PARTIAL CIRCULATION EXPERIMENTS WITHOUT OCCLUSION OF THE VENAE CAVAE

A series of experiments was performed to observe the effect upon animals of continuous passage of a part of their circulating blood volume through the apparatus. The apparatus was prepared as described before. Dogs of 10 to 25 kilograms of body weight were anesthetized with sodium pentothal intravenously, 25 milligrams per kilogram of body weight. Under sterile conditions, a cannula was inserted cephalad in the right femoral artery and the right auricle was cannulated through the right external jugular vein with a glass cannula 12 centimeters long and 3.5 millimeters in internal diameter. Venous blood was continuously withdrawn from the dog's right auricle, exposed to 100 per cent oxygen in the revolving cylinder, and returned to the animal at the same rate through the femoral artery. The venae cavae were not clamped.

Eleven of these experiments were performed. From 5 to 43 milliliters of blood per kilogram of body weight per minute were withdrawn from the right auricle, passed through the apparatus and continuously injected into the femoral artery for periods varying from 81 to 188 minutes. These animals lived less than 12 hours, exhibited no reflexes and died in coma. At postmortem examination multiple small emboli were found throughout the viscera. No other cause for the deaths of these dogs could be found.

Three pairs of experiments were performed to determine whether the lungs might be used to filter these small emboli from the blood. Seven hundred milliliters of blood were drawn from a donor dog and recirculated for one-half hour through the apparatus at a moderate rate of flow, 225 milliliters per minute. One-half of this blood was injected *intravenously* at a rate of 20 milliliters per minute into a dog anesthetized with sodium pentothal, without ill effect. The other 350 milliliters of blood, injected at the same rate *intra-arterially* into a similarly anesthetized dog, resulted in the death of the animal. The same results were obtained in the other two paired experiments. It appeared, therefore, that the lungs act as an efficient filter for small embolic particles in the blood.

It was thought that arterial embolic phenomena might be avoided if the donor animal's blood, which had been recirculating in the apparatus, was filtered through the lungs of the animal to be perfused before injection into an artery. This hypothesis was tested in 7 experiments by passing the donor blood through the perfused animal's lungs in the initial part of each experiment. An additional 4-way stopcock was placed in the circuit which enabled the flow of blood from the venae cavae and to the femoral artery to be reversed. Thus, the venous pump continually withdrew blood from the femoral artery and the arterial pump simultaneously reinjected it at an equal rate into the venae cavae during the first 5 minutes of a 30 to 40 minute perfusion. The stopcock was then turned so as to restore the customary direction of blood flow through the circuit. In this way the donor blood was filtered through the animal's lungs before the arterial perfusion was begun. However, there was no further filtration of the blood which passed into the animal's arterial system during the rest of the perfusion. All 7 of these dogs died during or following perfusion. The autopsy findings were similar to those in animals which received unfiltered blood from the apparatus. Thus, it

appeared that preliminary filtering of the donor blood through the lungs was not sufficient to prevent death from multiple small emboli.

It appeared necessary, therefore, to pass the blood through some mechanical filter before injecting it into an artery. A monel metal filter, similar to that described by Bjork (4), with a 300 by 300 micron mesh and thread thickness of 140 microns, was put in the circuit (Fig. 3, and Fig. 2, *I*). The donor blood used to fill the extracorporeal circuit was recirculated through the apparatus for approximately 15 minutes prior to perfusion, so that all of it passed through the filter several times. During the perfusion this filter provided continuous filtration. In long experiments the filter became coated on both inner and outer surfaces with a gray gelatinous layer, which appeared microscopically to consist of fibrin and disintegrated cells. The filter did not appreciably increase hemolysis.

With the filter in the circuit, 6 consecutive partial circulation experiments were performed with survival of all the animals (Table I). The largest blood flow (0–140) through the apparatus was 401 milliliters per minute (26.8 ml. per kgm. per minute). In another experiment (0–142) approximately 350 milliliters of blood per minute (14.5 ml. per kgm. per minute) were pumped through the extracorporeal circuit for 2½ hours. The volume of blood passed through the apparatus in this experiment was 53,592 milliliters. Recovery of all 6 animals was rapid and uncomplicated. The 6 dogs were sacrificed from 42 to 106 days after perfusion. At autopsy there was no evidence of infarction or other organic damage in any of the 6 animals. One of the dogs, which was sacrificed because of the presence of severe mange on the forty-third day following perfusion, was found to have only one kidney. Its recovery had been without renal complications.

These experiments demonstrate that with continuous filtration a part of the circulating blood volume of dogs can be continuously passed through the apparatus for a period of as long as 2½ hours and this procedure be followed by prolonged survival of the dogs in a healthy condition.

Fig. 3. Photograph of the filter used in all successful perfusion experiments.

TOTAL CIRCULATION EXPERIMENTS WITH OCCLUSION OF THE VENAE CAVAE

To demonstrate that an apparatus can supplant, temporarily but completely, the functions of a dog's heart and lungs, the blood flow through these organs must be interrupted. In the following experiments this was done by occluding the superior and inferior venae cavae at their junctions with the right auricle. Under these circumstances the only blood entering the right side of the heart is that from the coronary veins.

Because a thoracotomy was necessary to occlude the venae cavae, it seemed expedient to insert large cannulas directly into the cavae to obtain a maximum flow of venous blood. In 4 experiments small incisions were made in the

TABLE I.—PARTIAL PERFUSION WITH FILTRATION OF BLOOD AND SURVIVAL OF DOGS

Experiment number	Weight of dog kgm.	Blood flow		Duration continuous partial perfusion min.	Total volume blood passed through apparatus ml.	Duration survival before sacrifice days
		ml./min.	ml./kgm. per min.			
0-135	24	225	9.4	40	9,000	106
0-138	18	264	14.7	60	15,840	53
0-139	16	166	10.4	91	15,106	43
0-140	15	401	26.8	60	24,060	42
0-141	11	266	24.1	120	31,920	50
0-142	24	348	14.5	154	53,592	46
Average	18	278	16.7	87.5	24,920	57

superior and inferior venae cavae and wide bore glass T tubes were introduced into these vessels. Once tied into place in the cavae, blood could flow through the horizontal limb of the T tubes to the heart and lungs until the cavae were occluded by bulldog clamps between the tubes and the heart. When the cavae were occluded, blood was withdrawn by the venous pump through the vertical limbs of the T tubes and the cardiorespiratory functions were entirely maintained by the extracorporeal circuit. Adequate rates of flow were obtained, but the method was discarded for 3 reasons. First, at the end of the period of perfusion, in order to remove the cannulas, it was necessary to clamp the venae cavae until Pott's clamps could be applied to repair the vessels. The animals withstood poorly this brief interim of total occlusion without an artificial circulation. Second, the wounds in the venae cavae continued to ooze in the heparinized animal, and third, the procedure was time consuming.

The following technique was found practical and satisfactory. Through a right thoracotomy, the venae cavae were isolated close to the pericardium and braided silk ligatures were passed loosely about them. The superior vena cava was cannulated by way of the azygos vein. The azygos vein was ligated at its junction with the superior intercostal vein and a curved metal cannula introduced proximal to the ligature. The cannula was inserted medially through the azygos vein into the superior vena cava where its orifice was directed cephalad. It was then tied in place in the azygos vein (Fig. 4). The inferior vena cava was cannulated by way of the right auricular appendage. The pericardium was opened, the right auricular appendage grasped, and a curved cannula was inserted via a small incision in the appendage through the right auricle into the inferior vena cava where its orifice was directed caudad. It was then tied in place in the auricle.

These thin walled, stainless steel cannulas were filled with sterile physiological saline prior to insertion. The external diameters of the cannulas in the superior and inferior venae cavae were 5 and 6 millimeters respectively. In dogs of 6 to 11 kilograms cannulas of this size did not obstruct the return of venous blood to the heart until the ligatures around the venae cavae were tied over the cannulas. When it was desired to stop the flow of blood to the right side of the heart, the braided silk ligatures previously placed around the cavae, were tied tightly over the cannulas (Fig. 4). In this way the entire flow of venous blood could be diverted from the dog's heart and lungs to the extracorporeal circuit, which then assumed the functions of the cardiorespiratory system.

The operations were performed under sterile conditions. Adult mongrel dogs, weighing 6 to 11 kilograms were anesthetized with sodium pentothal (25 mgm. per kgm. of body weight) intravenously, and a flexible tube with an inflatable rubber cuff was inserted into the trachea. Oxygen was introduced through a rubber catheter into the tracheal tube at a rate of 2 liters per minute. Because of the light general anesthesia, local anesthesia, 1 per cent procaine, was used for both the thoracic and femoral incisions. Before the perfusion of the dog was begun, the depth of anesthesia was increased by an additional dose of 10 milligrams of sodium pentothal per kilogram of body weight. Usually no additional sodium pentothal was required during a 30 to 45 minute perfusion period.

The right femoral artery was cannulated for return of oxygenated blood from the apparatus. The left femoral artery was cannulated for direct blood pressure measurement with a mercury manometer. The stainless steel can-

nulas were thin walled and of as large a bore (2.5 to 4.0 mm.) as the lumen of the arteries would admit. Each was connected to a short piece of rubber tubing filled with physiological salt solution containing a small amount of heparin. The endotracheal tube was connected to a positive pressure respirator and the lungs were intermittently insufflated 8 to 12 times a minute with air at a pressure of 15 centimeters of water. The right pleural cavity was then opened either through an incision in the fourth interspace or through the bed of the fourth rib, and the venae cavae were cannulated as described. Heparin was given intravenously, 5 milligrams per kilogram of body weight, after the operative procedures had been completed and immediately before the perfusion was commenced.

To connect the extracorporeal circuit with the dog's own vascular system, the stopcock, *N*, Figure 2 was turned one quarter of a circle. At the same time the gas flowing into the oxygenating cylinder was changed from 96 per cent oxygen and 4 per cent carbon dioxide to 100 per cent oxygen. The output of the venous pump, *A*, was slowly increased until the venae cavae were almost collapsed. The braided silk ligatures about the venae cavae were then tied tightly over the venous cannulas, diverting all the blood returning to the heart through these vessels to the extracorporeal circuit. After the cavae were occluded it was usually possible to increase the venous pumping rate if the cannulas were carefully aligned in the center of the cavae.

During the period of occlusion of the venae cavae the heart appeared smaller. The rhythm was regular and the rate usually varied between 100 and 115 per minute. The myocardium, which was receiving oxygenated blood through the coronary arteries, did not change in color during the perfusion, but the lungs blanched noticeably after the cavae were occluded. The corneal reflex was often lost during perfusion but the lid reflex usually remained intact and occasionally the animals moved their heads. The color of the buccal mucosa was pink. Several dogs voided clear colorless urine during or shortly after the period of perfusion. Rectal temperature was maintained at approximately 36 degrees C.

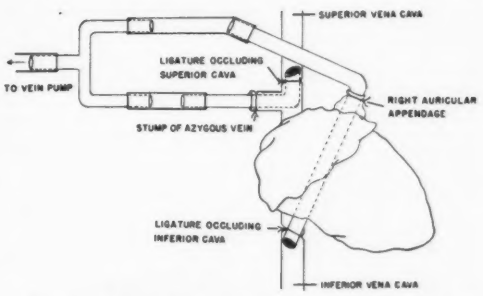

Fig. 4. Diagram showing the method of cannulating the superior and inferior venae cavae. When the ligatures about the superior and inferior venae cavae were tied, all blood returning to the animal's heart was diverted to the extracorporeal circuit.

On termination of the perfusion it was possible to restore the cardiorespiratory functions to the animal's own heart and lungs abruptly. The ligatures about the cavae were cut and removed and partial circulation was maintained for 3 or 4 minutes, until the cannulas could be removed from the cavae and the auricular appendage and azygos vein ligated. A search for small bleeding vessels was made and the chest closed in layers. Positive pressure breathing was then discontinued. A small soft rubber catheter was usually left in the right costophrenic angle. Blood which was removed through this catheter was transfused intraarterially. After the arterial cannulas were removed, the femoral arteries were ligated and the wounds were closed. At the conclusion of the period of perfusion, protamine[1] was given the animal to decrease the coagulation time. One milligram of protamine was given for each milligram of heparin the animal had received.

The dogs usually reacted from anesthesia within 3 to 4 hours and were able to drink water and stand shakily within 6 to 8 hours. The hind legs were cooler than the forelegs for the first 2 days after operation, but no difficulties were encountered from the bilateral ligation of the femoral arteries (7,52). Rectal temperature for the first 48 hours after perfusion varied between 38 degrees C. and 40 degrees C. Penicillin, 100,000 units, was given

[1]The protamine sulfate used was in 5 milliliter ampules, 0.1 per cent strength. This was diluted to 0.025 per cent, and 5 milligrams per kilogram body weight were given over a 10 minute period.

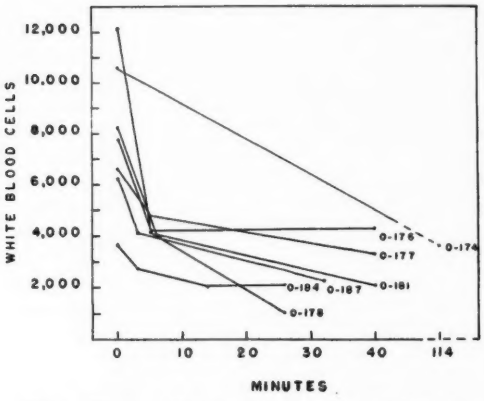

Fig. 5. Change in leucocyte count during perfusion experiments.

intra-arterially at the end of the perfusion, then intramuscularly each day for the first week.

OBSERVATIONS ON THE BLOOD DURING PERFUSION

Red and white blood cell counts, hematocrit readings, and measurements of free hemoglobin in the plasma with an Evelyn colorimeter were made just before and at intervals during the perfusion. The blood gases were measured by the Van Slyke manometric method and the Roughton-Scholander technique. Determinations were done in duplicate, the maximum difference between duplicate samples being 0.20 volumes per cent for oxygen and 0.50 volumes per cent for carbon dioxide. Blood *p*H was determined with glass electrodes.

Injury to blood cells. There was a decrease in the leucocyte count in all experiments. The granulocytes were more affected than the lymphocytes. After a sharp decrease in the leucocyte count within the first 5 minutes of perfusion, the count dropped slowly during the next 30 to 40 minutes. This trend is indicated graphically in Figure 5. The greatest change was a decrease from 12,500 cells per cubic millimeter to 1,050 cells per cubic millimeter during 26 minutes of perfusion. The smallest decrease was from 3,650 to 2,100 cells per cubic millimeter, also during 26 minutes of perfusion.

The red cell count and hematocrit readings did not change significantly during passage of the blood through the circuit. However, some slight hemolysis always occurred. The hemolysis induced during 45 minutes of animal perfusion varied from a minimum of 150 milligrams of hemoglobin per 100 milliliters of plasma to a maximum of 550 milligrams of hemoglobin per 100 milliliters of plasma (Fig. 6). The level at which free hemoglobin in the plasma first produces a faint pink color is about 60 milligrams per 100 milliliters of plasma. In 1 experiment after 111 minutes of perfusion, there were 400 milligrams of hemoglobin per 100 milliliters of plasma. The greatest amount of hemolysis induced in any of the surviving animals was 198 milligrams per 100 milliliters of plasma during 38 minutes of perfusion while the cavae were clamped for 33 minutes. Hemoglobin was not found during or after perfusion in the urine of any of the surviving dogs, and none of the animals died of anuria.

Oxygenation. The blood was sometimes inadequately oxygenated during its passage through the extracorporeal circuit. Table II lists 7 perfusion experiments in which blood gas and *p*H determinations were made on blood samples taken before and during complete occlusion of both venae cavae. Four of these animals died and 3 lived. The volume of oxygen introduced during perfusion of the 4 animals that succumbed varied from 39.8 cubic centimeters per minute to 43.7 cubic centimeters per minute. Two of these animals showed distinct signs of cerebral anoxia after perfusion. The volume of oxygen introduced in the 3 surviving animals was 43.0, 50.1, and 57.5 cubic centimeters per minute, and there were no signs of cerebral anoxia. The venous blood oxygen saturation in these 7 experiments ranged from 41 to 63 per cent, and the saturation of the arterial blood from 66 to 100 per cent. The rate of blood flow in the 4 dogs that died (Table II) was 60, 64, 78, and 95 milliliters per kilogram per minute, whereas the rate of blood flow in the 3 surviving animals was 85, 102, and 127 milliliters per kilogram per minute.

Carbon dioxide elimination and acid-base balance. During perfusion with the venae

cavae occluded the *p*H of the blood lay between 7.39 and 7.74 (Table II). Between 37.7 and 57.2 cubic centimeters of carbon dioxide left the blood per minute. With 1 exception (Exp. 0–179) the carbon dioxide tension of the arterial blood was quite low before perfusion. This was probably due to hyperventilation of the animals' lungs during the operative preparation with an open thoracotomy. Despite this initial low level, the carbon dioxide tension remained constant or decreased during perfusion with the complete occlusion of the venae cavae.

RESULTS

The venae cavae of 39 dogs have been clamped for periods up to 1 hour and 53 minutes, while the extracorporeal circuit maintained life in the animals' tissues. These 39 experiments fall into 3 groups. In the first group of 30 animals the venae cavae were occluded for periods up to 35 minutes. Seven of these animals survived periods of circulatory arrest of 30 to 35 minutes. In the second group there are 6 dogs in which the venae cavae were clamped for from 35 to 47 minutes. One of these animals survived a period of caval occlusion of 46 minutes. In 3 experiments the venae cavae were clamped for 60 to 113 minutes. All 3 of the dogs in these experiments died.

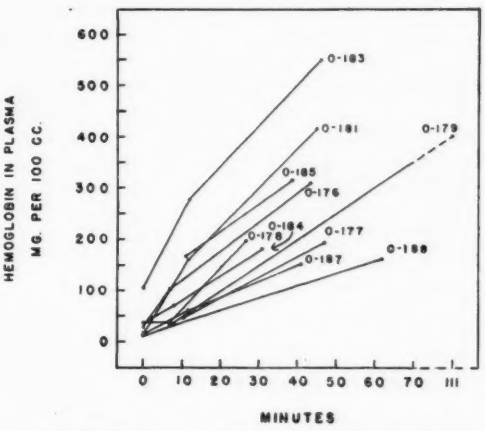

Fig. 6. Hemolysis during perfusion experiments.

A large proportion of the deaths occurred in the early phase of the investigation. Several of the animals whose blood had been heparinized died of hemorrhage. Experience with the use of protamine and meticulous hemostasis has largely decreased this danger. Maintenance of a physiologic acid-base balance became possible only after the proper use of carbon dioxide in the aerating mixture was learned. Some deaths were due to mechanical difficulties with the apparatus. The most fre-

TABLE II.—BLOOD GAS AND *p*H DETERMINATIONS WITH COMPLETE OCCLUSION OF VENAE CAVAE

Exper. No.	Wt. of dog kgm.	When blood sample was taken	Oxygen saturation		Oxygen added to blood c.c./min.	CO_2 removed from blood c.c./min.	*p*H arterial blood mm. Hg	CO_2 tension arterial blood mm. Hg	Blood flow ml./kgm. per min.	Result
			Venous per cent	Arterial per cent						
0-178	7.8	Before perfusion		96	57.5	39.8	7.41	28	102	Survived
		After 25 minutes' perfusion	43				7.74	9		
0-179	7.9	Before perfusion		94	40.5	39.9	7.30	41	64	Died
		After 28 minutes' perfusion	41	87			7.39	19		
0-184	6.1	Before perfusion		96	43.0	37.7	7.61	15	127	Survived
		After 26 minutes' perfusion	63	100			7.44	16		
0-187	10.0	Before perfusion		92	48.2 50.1	57.2 43.4	7.54		85	Survived
		After 12 minutes' perfusion	57	94			7.57	17		
		After 32 minutes' perfusion	50	87			7.50	19		
0-188	7.3	Before perfusion		94	43.7	50.3	7.54	23	95	Died
		After 60 minutes perfusion	53	92			7.49	18		
0-194	11.0	Before perfusion		87	39.8	50.9	7.50	31	78	Died
		After 24 minutes' perfusion	42	66			7.54	21		
0-196	9.0	Before perfusion		92			7.56	17	60	Died
		After 18 minutes' perfusion		81			7.50	17		
Average		Before perfusion		93	46.1	45.6	7.49		87	
		After perfusion	50	88			7.52			

TABLE III.—ANIMALS SURVIVING COMPLETE OCCLUSION OF VENAE CAVAE

Exper. No.	Date 1949	Weight of dog kgm.	Total occlusion of venae cavae minutes	Time artificial circulation continued after release minutes	Total duration artificial circulation minutes	Blood flow		Duration of survival days	Cause of death
						ml./min.	ml./kgm. per min.		
0-159	March 24	9.0	30	3	36	756	84	306+	
0-167	April 7	9.3	30	2	35	812	87	22	Accidental
0-177	May 2	9.8	32	10	47	890	91	25	Pericardial effusion
0-178	May 4	7.8	33	2	38	792	102	5	Cerebellar hemorrhage (sacrificed)
0-182	May 13	6.4	33	2	40	747	117	257+	
0-184	May 18	6.1	32	2	39	774	127	252+	
0-186	May 23	9.0	46	5	56	854	95	23	Pericardial effusion
0-187	May 25	10.0	35	9	67	854	85	245+	
Averages		8.4	34	4.4	45	810	99		

quent cause of death, however, was anoxia due first to inability to withdraw a volume of blood from the cavae equivalent to the animal's cardiac output, and, second, to failure of the present oxygenator to saturate this blood with oxygen.

The longest period during which the venae cavae were completely occluded and life was maintained by the extracorporeal circuit was 113 minutes. There is no reason to assume, however, that cardiorespiratory functions could not have been maintained for an even longer time. During the 113 minutes of perfusion the animal's heart rate remained regular and the blood was adequately oxygenated. Corneal reflexes were depressed but lid reflexes were active throughout. Function was restored to the animal's heart without arrhythmia at the end of the perfusion period. Respiration began immediately upon disconnecting the positive pressure apparatus. The animal died 2 hours after perfusion was stopped. Death of this dog was believed due to a period of hypoxia and hypotension immediately before perfusion.

The experimental data on the animals surviving complete occlusion of the venae cavae for from 30 to 46 minutes are summarized in Table III. Four of the 8 surviving animals died between 5 and 25 days following perfusion, and 4 are still alive, normal, and healthy. Dog 0–178 made a normal recovery following a period of caval occlusion of 33 minutes. The animal ate well, played with the other dogs and appeared to have no organic damage; however, on the evening of the fourth day he developed nystagmus, unsteadiness of gait and hyperpyrexia, and was sacrificed the next day. At autopsy a right cerebellar hemorrhage was found. None of the visceral organs showed signs of emboli. Dog 0–167 which had survived a 30 minute period of caval occlusion died 22 days later from severe injuries to the right chest and right hind leg sustained on the preceding day in an accidental fall from a tall laboratory table. It had shown no signs of organic damage following the perfusion and autopsy failed to reveal any evidence of embolic phenomena in any of the organs including the brain. Two dogs (0–177 and 0–186) died on the 25th and 23rd days following clamping of the venae cavae for 32 and 46 minutes respectively. Both these deaths were a result of pericardial effusion. The pericardial opening had been loosely approximated with one suture. The pericardial effusion in the animal that survived 46 minutes of caval occlusion (0–186) was diagnosed by fluoroscopy on the 15th day following perfusion, and was treated unsuccessfully by pericardiocentesis. Four days later, therefore, a right thoracotomy was done, the pericardial sac widely opened, and approximately 185 milliliters of serosanguineous fluid removed. The

animal recovered from this second operation but the pericardium became densely adherent to the heart; an effusion reaccumulated, resulting in the death of the animal on the 23rd day following perfusion. This 46 minute period of occlusion of both venae cavae is, we believe, the longest period ever reported during which cardiorespiratory functions have been completely maintained by an extracorporeal circuit, followed by survival of the animal. The 4 remaining surviving animals are now alive and well, between 8 and 10 months after the experiments.

DISCUSSION

For a mechanical heart and lung to take over temporarily a *part* of the cardiorespiratory functions, the following requirements should be met.

1. The blood returning to the subject from the apparatus should be saturated with oxygen.

2. The carbon dioxide tension, and thus the *p*H, of the blood returned to the subject should lie within a normal range.

3. Destruction of the cellular elements of the blood during its passage through the mechanical heart and lungs should be minimal.

4. The blood must be rendered incoagulable during its passage through the extracorporeal circuit and at the conclusion of the procedure blood coagulability should be restored.

5. The blood should be filtered before returning it to the subject if it is passed through an apparatus such as the one described in this report.

For a mechanical heart and lung to take over temporarily *all* of the cardiorespiratory functions, so as to permit operations to be performed within any of the cardiac chambers, the conditions listed should obtain and, in addition:

1. The flow of blood through the extracorporeal circuit must approximate the normal cardiac output of the subject. A pulsatile blood flow in the subject's arteries is apparently not necessary for the normal function of vital organs, at least for periods as long as 46 minutes.

2. *All* the blood returning to the heart through the venae cavae must be diverted to the mechanical heart and lung.

Oxygenation. Levy and Blalock found the oxygen consumption as measured by a Benedict spirometer in 13 unanesthetized dogs to be approximately 6 cubic centimeters per kilogram per minute. With the apparatus used in these experiments the maximum amount of oxygen which could be introduced into the blood was 70 cubic centimeters per minute (66). Consequently small dogs, 6 to 11 kilograms in weight, were used in all our experiments with occlusion of the venae cavae, in order not to exceed the capacity of the apparatus to introduce a sufficient amount of oxygen. The possibly contributory role of anoxia as a cause of death in our experiments can be seen by reference to Table II. In the 3 surviving animals 7.4, 7.1, and 5.0 cubic centimeters of oxygen were introduced per kilogram per minute. Three animals failed to survive when oxygen was introduced at 6.0, 5.1, and 3.5 cubic centimeters per kilogram per minute. Recently a much more efficient method of oxygenating blood has been used successfully and will be reported elsewhere (67, 68).

Kabat (41) found that the respiratory center of newborn dogs continued to function 17 times as long as the center of the adult animal during complete arrest of the cerebral blood flow. He and his co-workers (42) also reported that very young animals would tolerate arrest of the cerebral circulation for a period 4 times as long as that tolerated by an adult, followed by complete functional recovery. All the animals used in our experiments were older than 4 months, the age at which Kabat noted a decrease to the adult level in resistance to anoxia.

Acid-base balance. During recirculation of donor blood in the apparatus prior to perfusion a mixture of 4 per cent carbon dioxide and 96 per cent oxygen was blown over the blood film in order to keep the *p*H of the blood constant. When oxygen alone was used the *p*H rose in one experiment to 8.5 due to the washing out of carbon dioxide (Fig. 7). On the other hand, during perfusion, when the animal's metabolic carbon dioxide had to be removed, the use of 100 per cent oxygen proved necessary to wash out this carbon dioxide and keep the *p*H within a physiologic range (Fig. 8). In

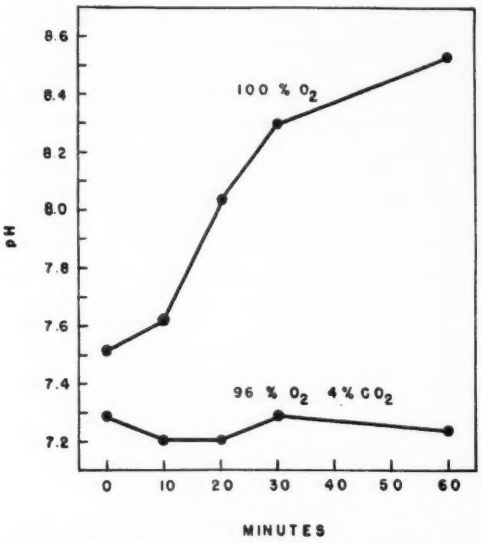

Fig. 7. The effect of carbon dioxide in the gas mixture on the *p*H of the blood recirculated in the apparatus.

3 experiments in which 4 per cent carbon dioxide was used in the gas mixture during perfusion of the animal, the carbon dioxide rose and resulted in severe uncompensated acidosis. In one such experiment the *p*H fell to 6.54 (Fig. 8) and the carbon dioxide tension of the blood rose to 284.5 millimeters of mercury. This animal died 5 hours later.

Bjork (4), using a mixture of 6.5 per cent carbon dioxide and 93.5 per cent oxygen in 8 brain perfusions, found it caused rather severe acidosis. On one occasion the *p*H fell to 6.75 after 1½ hours of perfusion. In 12 of his experiments pure oxygen was used and in addition 50 milliliters of isotonic 1.3 per cent sodium bicarbonate solution were added by drip to the blood. The use of 100 per cent oxygen caused an uncompensated carbon dioxide deficit with an increase in *p*H. Addition of bicarbonate permitted elimination of carbon dioxide without a concomitant decrease in plasma bicarbonate. Bjork's object was to produce an alkaline urine, and in this manner to prevent the deposition of acid hematin in the renal tubules.

Hemolysis. Hemolysis may cause renal insufficiency and anuria. Yorke and Nauss were among the first to attribute the mechanism of renal insufficiency from hemoglobinuria to the blocking of the tubular lumina by cellular débris and hemoglobin derivatives. DeGowin and others believe that in addition to the mechanical blockage there is a nephrotoxic factor which causes interstitial edema and degeneration of tubular epithelium. In their experiments both processes could be eliminated by alkalinizing the urine. A filtered stroma-free solution of hemoglobin, however, is not toxic. Amberson (1) found that animals would tolerate the replacement of 80 per cent of their normal blood volume with hemoglobin-Ringer's solution containing 12 to 14 per cent hemoglobin, and O'Shaughnessy (57) introduced as much as 600 cubic centimeters of 5 per cent hemoglobin-Ringer's solution over a 30 minute period to a female patient "without untoward after effects." Although a filtered solution of hemoglobin is not toxic, and alkalinization of urine may prevent deposition of unfiltered hemoglobin derivatives in the renal tubules, great care was taken to minimize hemolysis in our experiments. The pumps in the present apparatus were constructed so that the rollers do not completely compress the tubing. Thus there can be no grinding of the cells between the apposed surfaces of the rubber tubing. The spout through which the blood enters the oxygenating cylinder directs the blood tangentially against the inner surface of the cylinder. The stationary collecting cup at the bottom of the revolving cylinder was also constructed so that passage of the blood film from the surface of the cylinder to the surface of the cup takes place with minimal damage to the blood cells.

The level at which hemoglobinuria occurs in dogs has been investigated by Manwell and Whipple, who found hemoglobinuria when hemoglobin was injected intravenously in amounts varying between 190 and 250 milligrams per kilogram of body weight. Lichty and associates, using more accurate methods, found that hemoglobinuria occurred following the intravenous injection of 124 to 210 milligrams of hemoglobin per kilogram of body weight. The renal threshold of hemoglobin in man was investigated by Gilligan and others, who injected filtered hemoglobin solutions in-

travenously and found hemoglobin in the urine of all normal subjects when the plasma hemoglobin was above 135 milligrams per 100 milliliter. At lower levels hemoglobin did not appear in the urine. The hemolysis observed in our experiments with surviving animals did not exceed 200 milligrams of hemoglobin per 100 milliliters of plasma, and none had hemoglobinuria during or after perfusion. From these experiments it seems that hemolysis is not likely to be a major impediment to the successful perfusion of man (2).

Blood clotting. A single large initial dose of heparin prior to perfusion renders the blood incoagulable for the duration of an experiment. Postoperative intrathoracic bleeding was a contributory cause of death in several of the early experiments. Very careful hemostasis was used and protamine, 5 milligrams per kilogram of body weight, was given at the conclusion of perfusion to restore normal blood coagulability. None of the surviving animals developed hematoma, although there was always some collection of serosanguineous fluid in the right pleural cavity. Chargaff and Olsen (10) found that protamine could be used to counteract the effect of heparin, both in vitro and in vivo. Protamine was further studied in man by Jorpes, Edman, and Thaning. Although protamines neutralize heparin, they also have anticoagulant properties, due to (a) an antithromboplastic action (11, 71); (b) antiprothrombic activity (23); and (c) precipitation of fibrinogen (53). For neutralization to occur a quantitative relationship must exist between the protamine introduced and heparin present. Parkin (58) suggests a ratio of approximately 1.5 milligrams of protamine to 10 milligrams of heparin. Otherwise a prolongation of coagulation times was found. Jaques and Waters found that protamine neutralizes heparin in the ratio of 1.9 to 3.0 milligrams of protamine to 1.0 milligram of heparin. Parkin and Kvale (59) found a transient drop in blood pressure when 2.0 milligrams of protamine per kilogram body weight were given to anesthetized dogs, but no change in blood pressure when the same dose was administered to unanesthetized dogs. They also found that the intravenous injection of 40 to 50 milligrams of protamine in patients

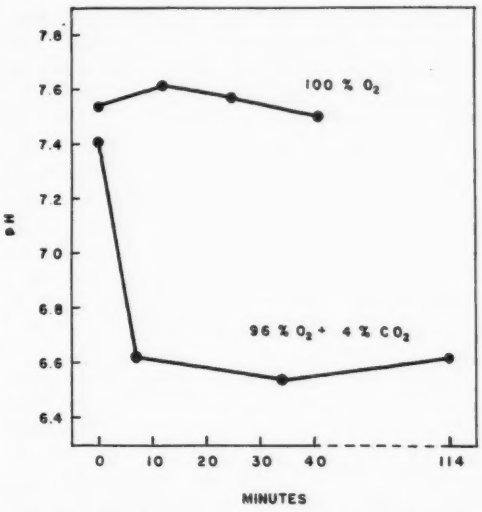

Fig. 8. The effect of carbon dioxide in the gas mixture on the *p*H of the blood during perfusion of dogs.

neutralized the effect of 50 milligrams of heparin and, when given slowly, produced no reactions. We have used 1 milligram of protamine per milligram of heparin and found that if the protamine was given rapidly or in concentrations greater than 0.025 per cent, a fall in blood pressure of 40 to 80 millimeters of mercury consistently occurred. When the same amount of protamine in dilute solution was administered over a 10 minute period, no drop in blood pressure or other undesirable effects were noted.

Filtration of perfused blood. Most investigators have found it necessary to filter blood used for perfusion. The following devices have been used separately or in combination: coarse muslin, cotton wool, cambric filters, glass wool, fine linen, platinum screens, or the lungs of an animal. Daly and Thorpe believed filtration of blood used for perfusion was essential to prevent cardiac failure caused by occlusions of the coronary vessels with cellular débris, or by vigorous and protracted constriction of these vessels.

Bjork reported the death of 11 animals during or after brain perfusion before he inserted a filter into his apparatus. In each instance the brain appeared to have been damaged

although the blood leaving the perfusion apparatus was well oxygenated (91 to 100 per cent saturation). "Nor could any other definite reason for the damage to the brain be ascertained by analysis of the blood" (4). Before perfusion Bjork filtered the blood from donor dogs, first through a monel metal filter with a mesh of 150 by 150 microns and then through the subject dog's own lungs before commencing perfusion of the brain. In addition, continuous filtration of the blood was provided by the inclusion in the circuit of a nickel filter which is provided with 300 by 300 micron mesh.

Successful perfusions, however, have been performed without filtration. Bjork was able to perfuse the brain of one dog for 1½ hours with unfiltered blood, without evidence of cerebral damage (4). Gibbon in 1939 successfully perfused cats without filtration of the blood during periods of occlusion of the pulmonary artery (27).

Before a filter was inserted into our apparatus, 11 animals died following periods of partial circulation. With a filter in the circuit, 6 partial circulation experiments were performed followed by prolonged survival of the animals without vital or postmortem evidence of organic damage.

Cardiac output. A blood flow through the extracorporeal circuit approximating normal cardiac output is obviously desirable. Gibbon found an average blood flow of 99 milliliters per kilogram per minute would maintain a normal blood pressure during perfusion of cats (27). Dogs anesthetized with sodium barbital have been reported to have a cardiac output of approximately 170 milliliters per minute (31, 36). Levy and Blalock using the Fick principle, found an average cardiac output of 112 milliliters per kilogram per minute in 13 unanesthetized dogs. The average blood flow through the circuit during occlusion of the venae cavae in the 8 surviving dogs reported here was 99 milliliters per kilogram per minute.

The earlier physiological literature contains a number of references to the value of pulsation while perfusing isolated organs. Patients with coarctation of the aorta frequently have such a markedly diminished pulse pressure below the coarcted area that no pulsation is palpable in the arteries of the lower extremities, or in the abdominal aorta. Under these circumstances, however, the abdominal organs appear to function normally. A pulsatile blood flow was not used in the experiments reported here.

Complete maintenance of cardiorespiratory function. It is important in reporting investigative work in this field to distinguish between experiments in which only a part of the circulation is carried by an extracorporeal circuit, and those in which the venae cavae are clamped and all the blood returning to the heart through these vessels is diverted to the extracorporeal circuit.

The diversion of only a part of the venous return to the heart from the venae cavae to a mechanical heart and lungs is a relatively simple procedure. Jongbloed (39) and Dennis have reported such experiments. The 6 consecutive experiments listed in Table I demonstrate that it is quite possible to take over a part of the cardiorespiratory functions by means of a mechanical heart and lungs without detriment to the subject animal. Thus it would appear that animal experimentation has shown the feasibility of carrying a part of the cardiorespiratory functions by mechanical means, and the clinical application to human patients will be undertaken in the near future.

To open the chambers of the heart for operative procedures, the venous return to the heart by way of the venae cavae must be *completely* diverted. With both venae cavae clamped at their junction with the right auricle, the only impediment to a bloodless operative field within the cardiac chambers will be the blood entering the right side of the heart through the coronary sinus and the coronary veins. This blood will obviously have to be aspirated during the operative procedure and returned to the extracorporeal circuit. It appears to us to be just as important to supply the myocardium with oxygenated blood as to supply other organs such as the liver and kidney. Indeed, in cases in which the heart is already handicapped by a congenital malformation, or by diseased valves, the maintenance of the coronary circulation is of particular importance.

In the experiments reported here the myocardium continuously received oxygenated blood from the aorta by way of the coronary arteries. Even when the extracorporeal circulation was suddenly stopped and the burden of the entire circulation was abruptly restored to the animal's heart, there was no drop in blood pressure or disturbance of cardiac rhythm. There was often a rise in blood pressure of 10 to 15 millimeters of mercury following cessation of the extracorporeal circulation and removal of the cannulas in the venae cavae. Ventricular fibrillation never occurred. On the other hand, Bjork perfusing only the brain of the animals in his experiments cited some difficulty in reinitiating cardiac function. He reported the death of one dog as a result of ventricular fibrillation and frequently observed dilatation of the heart when clamps were removed from the venae cavae (4).

Role of the mechanical lung. In order to operate within the chambers of the heart under direct vision, the flow of blood to the side of the heart being operated upon must be diverted. Wherever a defect in the septum between the 2 sides of the heart exists, the blood flow must be diverted from both sides of the heart. When no septal defect is present, it is conceivable that the right side of the heart might be opened for an operative procedure by diverting the flow of blood from both venae cavae around the right side of the heart and injecting it into the pulmonary arterial system. Indeed, Sewell and Glenn have described a pump for such a purpose. Again in the absence of septal defects, the left side of the heart might also be opened for operative procedures by shunting the blood returning to the left auricle from the pulmonary veins into the systemic arterial system. Here also, a single mechanical pump is all that would be required. Finally, it is conceivable that either side of the heart might be opened in the presence of a septal defect provided the blood returning to the right side of the heart were short-circuited by a mechanical pump directly into the pulmonary arteries, and that returning to the left side of the heart from the lungs was diverted directly into the systemic arteries. Two pumps would be required for such a double extracorporeal circuit.

The advantages of using only a pump, or pumps, to short-circuit blood around the right or left side of the heart, or both, lies in the fact that the difficulties entailed in a mechanical lung are eliminated. Also where the shunt is from venae cavae to pulmonary artery the lungs will act as a filter for emboli. However, such methods would entail the opening, cannulation, and subsequent closure by suture, of many large vessels within the chest that are not involved in the use of a mechanical heart and lung such as we have described. Moreover, dispensing with a mechanical lung would not eliminate the problem of hemolysis or the problem of performing an operation when the blood has been rendered incoagulable by heparin.

It is obvious that the first clinical application of extracorporeal circuits will be to take over a part of the burden of circulation in patients with acute failure of the cardiac or respiratory functions. In conditions such as pulmonary edema, or coronary thrombosis the blood can be withdrawn from a peripheral vein and returned to the body through a peripheral artery. The value of relieving the heart and lungs of part of their burden by such a procedure will obviously be greatly diminished unless a mechanical lung is in the extracorporeal circuit. In fact, the injection of venous blood into the systemic arteries might even be detrimental to the patient. Thus an extracorporeal circuit must include a mechanical lung to be of value in these conditions.

As regards intracardiac operations, it appears obvious that where septal defects are present, the use of a mechanical lung will greatly simplify the operative procedure. Where septal defects are absent it is possible that the elimination of a mechanical lung from the extracorporeal circuit might, at the present stage of development, simplify an operative procedure within the chambers of the right heart. The approach to the left side of the heart, without using a mechanical lung, appears to us to present technical difficulties which, while not insurmountable, may easily be as great as those entailed in the use of a mechanical lung. The importance, therefore, of developing and perfecting an extracorporeal circuit that can take over the function of not

only the heart but also the lungs, seems to us unquestionable.

SUMMARY

1. The object of developing an extracorporeal blood circuit capable of temporarily performing the functions of the heart and lungs is twofold. First, such an apparatus might be livesaving by maintaining a portion of the circulation temporarily where the function of either the heart or lungs is critically impaired. Second, such a device, if capable of maintaining all the cardiorespiratory functions, might permit the performance of intracardiac operations under direct vision, without fatal hemorrhage.

2. A mechanical heart and lung for such purposes has been described.

3. In 6 consecutive animal experiments blood was continuously withdrawn from the venae cavae, passed through the apparatus and continuously returned to the animal by way of a peripheral artery, for periods varying from 40 minutes to over 2½ hours. All 6 animals survived this procedure and showed no evidence of organic damage, either clinically or at autopsy some months later. In these 6 dogs only a part of the circulation was carried by the apparatus, and the venae cavae were not occluded.

4. Eight dogs have survived periods of complete occlusion of the venae cavae varying from 30 to 46 minutes. During occlusion of the venae cavae the entire cardiorespiratory functions were maintained by the apparatus. Four of these dogs have subsequently died. The 4 remaining dogs are still alive and entirely healthy, from 8 to 10 months later. The 46 minute period of occlusion of the venae cavae is, we believe, the longest reported during which the cardiorespiratory functions have been completely maintained by an extracorporeal circuit followed by survival of the animal.

5. We believe that the experiments reported here constitute a step forward toward the clinical application of such an apparatus in the temporary maintenance of a part of the cardiorespiratory functions in patients with a failing heart or lungs, as well as toward the ultimate goal of maintaining completely the cardiorespiratory functions so as to permit the performance of precise operations within the chambers of the human heart under direct vision in a bloodless field.

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WHOLE THICKNESS SKIN GRAFTS IN THE TREATMENT OF HERNIAS

Analysis of 211 Cases

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SOME three and one-half years ago, in May, 1946 to be exact, we used for the first time whole thickness skin grafts, as recommended by Mair, to repair hernias—inguinal, femoral, umbilical, and incisional.

It seems that the first to use skin without epidermis as grafts to repair postoperative hernias were Loewe in 1913 and Rehn in 1914. Later appeared the works and communications of Eitner in 1920, Eitel in 1924, Peer and Paddock in 1937, Uihlein in 1939, Cannaday in 1934, and others. In general the results were good, although some failures were reported, namely, recurrences and especially infections. The method had disadvantages too, for removal of the epidermis from the skin prolonged operation and also the graft usually must be taken from a zone distant from the hernia, and thus another scar is made.

To George B. Mair, a surgeon of Lanarkshire, Scotland, should go the credit for first, in 1938, having employed a whole thickness skin graft to repair an incisional hernia. Mair published a description of his technique in 3 important articles (6, 7, 8). He makes a distinction between the cutis graft, that is a skin graft without epidermis, and a whole thickness skin graft.

In Argentina we began using this technique at the Municipal Postgraduate Surgical School, which is under the direction of Professor Ricardo Finochietto. The details of the technique have been published elsewhere (10, 11, 13, 14, 15).

BASIC PRINCIPLES

Mair demonstrated clinically and experimentally that it is not necessary to strip the epidermic layer from the skin in order to use it as a graft. Separation of the epidermis from the dermis, a step formerly carried out because of the danger of infection from the epidermis, is not easy. Padgett's dermatome partly solves this difficulty, but in any case, no matter what technique is used, there might remain in the dermis the lower portion of a sebaceous gland or hair follicle which would make complete extirpation delusive. The fear that infection may be caused by potentially septic tissue such as the epidermis has not been confirmed in our practice; the 2.36 per cent of infections noted, a figure which coincides with that given by Mair, is not higher than the one reported for grafts of human or bovine fascia. Also the alleged danger of intolerance or of the formation of epidermic cysts is eliminated if the graft is *taultly fixed*, a fundamental requisite to obtain quick atrophy of the epidermis and of the sweat and sebaceous glands.

In the case of a recurrent inguinal hernia, the skin graft had become loose a few days after operation. At second operation we took a biopsy specimen and found epidermic cysts. It is important to note that the graft had become loose but in spite of the cysts it was well tolerated (Fig. 2 a, b, and c).

The possibility of obtaining the graft directly from the zone of the hernia is an evident advantage in favor of the whole thickness skin graft.

EVOLUTION OF THE GRAFT

It should be noted that during the first few days after operation the operative field is slightly reddish and infiltrated. This is not surprising; it indicates the reaction of the neighboring tissues to the presence of the graft and the autolytic process of the epidermic layers. This aspect, as Mair well states, which would seem to be a mild deep infection, is not accompanied by general phenomena, fever,

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malaise, as it is only an aseptic reaction, not an inflammation. In the cases in which drainage has been left as a precautionary measure, we observed that for several days a thick, dark liquid emerged. The histologic examination showed "leucocytary discharge." Repeated search for bacteria by means of the Ziehl-Neelsen and Gram-Koppeloff methods was negative, thus proving the absence of real pus. Gradually after the third week the slight tumefaction disappears, the graft becomes completely identified with the neighboring tissues, and has the appearance of a firm fibrous tissue resembling a scar or a strong aponeurosis.

In one case of incisional hernia in which we performed a second operation for another difficulty (obstruction) approximately 2 years after having applied a whole thickness skin graft, we took advantage of the opportunity to secure a small piece of the graft and found that it had become totally identified with the neighboring tissues. The pathologist, Dr. M. Polak, reported as follows: "The biopsy specimen includes the skin with its atrophic epidermis which in some zones consists only of three layers of cells. The malpighian elements present vacuolization phenomena and there is a remarkable hyperkeratosis. The sclerosed dermis is furrowed by thin blood and lymphatic capillaries, sometimes occupied by lymphocytes and monocytic elements. The elastic fibers, of a moderate thickness, are arranged in fascicles distributed irregularly (Fig. 1).

The findings in this examination are not exactly the same as those reported by Mair. However, the epidermic atrophy, dermal sclerosis, vitality of the graft (vascular neoformation), and finally the absence of epidermic cysts and other elements of intolerance are confirmed.

GENERAL TECHNIQUE FOR WHOLE THICKNESS SKIN GRAFTS

Conditions necessary for the graft. It is fundamental that the skin used for grafting be sound. The use of skin affected with acute or chronic infections, with parasitosis (sarcoptes, etc.), eczema, intertrigo, and the like, must be avoided; these conditions must be well treated and cured before the skin can be used for a graft. It is possible to use as grafts strong cicatricial skin, as we have done on some occasions, but skin furrowed with atrophic striations, "vergetures," should not be used as it is not sufficiently strong. We have proved this statement at operation and the premise has been confirmed also, from a histologic standpoint, by Dr. M. Polak, pathologist, who states: "Skin with atrophic and hyperkeratosic epidermis; in the vergetures the dermis presents nearly a total absence of elastic fibers." In other cases the pathologist found "a remarkable decrease and fragmentation of the elastic fibers." (Reports No. 10,821 and 11,204.)

We have used skin from the zone of operation, except in 6 cases. In 1 patient the skin was affected by repeated attacks of erysipelas; it was resected and rejected. In another, the skin had become thinned by atrophic striations, and in a third patient it was a very irregular scar with neighboring atrophic striations. In these 3 cases strong suitable skin was obtained from the anterior external region of the thigh.

Skin preparation. For 3 days prior to operation the zone of the hernia is carefully washed each day, followed by the application of 3 per cent iodine. We generally adhere to these instructions which Mair stressed as so important. This method of preparation was not possible in 6 patients with strangulated hernia and in a few patients operated upon as emergencies.

It is advisable to inject, a few moments before operation, a good prophylactic dose of penicillin: 200,000 to 500,000 units. On some occasions penicillin was used locally; it was injected diluted in the anesthetic solution.

Removal of the skin graft. With a scalpel, the outline of the graft is traced; care is used to include with the incision all of the dermis but to stop as soon as the adipose tissue is reached. The graft should be carefully dissected with the scalpel to separate it from the underlying fat. Dissection may be made easier by holding the edges of the graft with an Allis forceps or by keeping the graft tense over the left forefinger while the knife is being used (Fig. 3).

As to the extent and shape of the graft, it varies according to the size of the area to be covered. It should be remembered that skin is elastic and that apparently small pieces, tautly sutured, can cover surfaces larger than the original size of the graft. However, it is advisable to select a piece considered large and then eliminate the surplus.

Preparation of the graft. Once the graft is taken it is kept in normal salt or local anesthetic until it is used. This has the advantage that as the liquid absorbs any connective and adipose tissue that might remain adherent to the deep surface of the graft, its extirpation with a good pair of Mayo curved scissors is facilitated.

General technique of the operation. The operation must be carefully carried out. To avoid possible hematomas careful hemostasis must be accomplished. The vessels should be gently handled, the stumps must be small and the ligatures made with thin material. When the operation is carefully carried, little foreign material remains, and the graft will more readily adapt itself to its bed.

Placing the graft. Once the hernia has been treated, the bed where the graft will lie is prepared. The ideal bed is that made of muscular tissue. In inguinal hernias, the transversalis fascia covering Hessert's triangle constitutes the greater part of the bed. The deep surface of the graft must be applied to the bed. The edges of the graft are either sutured to fibrous tissue or aponeurosis. The stitches should be close; we place them every 4 or 5 millimeters apart. Mair prefers chromic catgut for suturing, we use cotton thread. Thin stainless steel wire is excellent. Unlike the suturing in other types of hernioplasties that in whole thickness skin graft repair must be done tautly; we compare the appearance of the graft with that of a drum parchment. When the graft is tautly sutured, atrophy of the epidermic layers and of the sweat and sebaceous glands is attained with absolute certainty. Once the graft is fastened, it should be covered, whenever possible, with an aponeurotic layer. Care must be taken to suture this layer loosely over the graft, because if it is tautly sutured the method loses its real value as the underlying graft becomes loose. It does not matter whether aponeurosis is used or whether it is too small to cover the graft; the skin is well tolerated even when covered with fat of the adipose cutaneous strips. Before the skin is sutured a solution of sulfanilamide or penicillin may be applied; preferably penicillin since sulfanilamide may encourage formation of serohematic effusion.

Postoperative. It is advisable to inject penicillin for 3 or 4 days. This is done in accordance with Mair's recommendations and we adhere to them not because we mistrust our aseptic technique but because, even if the skin graft is small, there is always the possibility of it being potentially septic.

Those who first used skin grafts kept their patients in bed 6 or more weeks after operation. Mair, using whole thickness skin, considers 3 weeks the optimum time. At first we adhered to this rule, then we reduced the period to 2 weeks for the large recurrent and incisional hernias and to 1 week for the smaller ones. At present we have shortened the time in bed even more; in some selected cases of inguinal hernias with grafts, the patient is kept in bed only 3 or 4 days.

SPECIAL TECHNIQUE

Inguinal hernia. Preferably local anesthesia is used; in the presence of very large or complicated hernias and as an exception, general or spinal anesthesia is employed.

To remove the graft an elliptical inguinal incision that circumscribes the classic operating line is made (Fig. 3). Mair considers that the minimum graft should be 7.5 by 2.5 centimeters in size. It has been our practice always to take larger grafts, 10 or 12 centimeters by 3 or 4 centimeters.

We wish to emphasize the necessity of following an impeccable operating technique, that is, high extirpation of the sac and, what for us is fundamental, the thinning of the cord as much as possible where it emerges from the deep inguinal ring, to eliminate the accessory elements—the fibrous connective tissue, lipomas, cremaster, and the like. In other words, we reduce the cord to its vital elements, the vessels and the vas deferens.

Except for some slight alterations, we follow the technique described by Mair for the

reconstruction. The ends of the graft are trimmed and an incision 3 to 4 centimeters in length is made in the portion of the graft that will become its external end. The transversalis fascia that covers the weakened zone (Hessert's or Hesselbach's triangle) is carefully folded and stitched to make it tense (Fig. 4). We apply the graft to its bed and then proceed to fasten it to the internal angle of the zone with a stitch that includes the fibrous tissue covering the pubis; with another stitch we fasten it to the lowest and external part of the rectus sheath and with a third stitch we fasten it to the innermost part of the crural arch or inguinal ligament (Fig. 5). We do not partially section the internal pillar as recommended by Mair.

Later, with the graft kept tense with an Allis forceps so as not to damage it, it is fixed, by means of sutures placed every 4 to 5 millimeters apart, to the inguinal ligament. To keep the graft taut it is advisable to grasp with each stitch a larger portion of the bed than of the graft and also to use the Andrews' suture (Fig. 6).

The cord, which has been properly thinned, is passed between the two pedicles of the extreme end of the graft. These pedicles are joined together with sutures, with great care not to strangulate the cord, and an orifice is formed through which the cord emerges well displaced upward (Fig. 7).

Within and above, the graft is fastened to the external border of the rectus sheath and to the aponeurotic portion of the internal oblique, and we sometimes also include in this suture the aponeurosis of the external oblique with the Andrews sutures. The upper external end of the graft is sutured to the muscle on which it rests, or better still, to the deep surface of the external oblique (Fig. 8). Over the graft the aponeurosis of the external oblique is laid and is loosely sutured together (Fig. 9). Should the edges not join properly, they are only partially sutured. The cord, as a result of the retrofunicular reconstruction remains subcutaneous.

In cases in which Poupart's ligament is naturally weak, or, as a result of previous operations, has been artificially weakened, we fasten the graft at its lower border to Cooper's ligament. To do this, the transversalis fascia is separated from the inguinal ligament, the preperitoneal fat is displaced and Cooper's ligament exposed; the graft is there fastened with 4 or 5 stitches, and on reaching the femoral vein is passed over it. Then the fixation is continued on the external portion of the inguinal ligament (Fig. 10). We have used this technique with excellent results in more than 15 cases.

In inguinal hernias which presented moderately weak walls and in which the use of a skin patch did not seem to be justified, the retrofunicular reconstruction was done in a single layer by means of a strip of skin about 3 millimeters wide removed when the incision was made. This technique has been described by our associate, M. J. Vazquez. To make the suturing easier we tie a piece of cotton thread to one end of the strip of skin and thread it to a strong needle. Sometimes we thread the strip directly through a small Gallie needle.

On 2 occasions we used the Anson MacVay technique, that is, liberation near the sheath of the rectus and fixation of the conjoined tendon to Cooper's ligament. To this the skin graft was added, it being laid over the muscular plane and being fixed below to Cooper's and the inguinal ligaments, inwardly to the border of the liberating incision, and above to the external oblique. Finally the graft is covered when the section of the external oblique is sutured.

INDICATIONS

Inguinal hernia. In primary inguinal hernias, whole thickness skin grafts should be used if the hernia is of the direct or indirect type with great weakness in Hessert's triangle, in sliding hernias if the voluminous neck has weakened and disorganized the tissue that could be used in the repair, in hernias of old patients whose tissues have little plastic power, and in general in every case in which the surgeon considers that the local elements are not capable of accomplishing the reconstruction with security. In milder cases in which the surgeon considers excessive the use of a skin patch but still wishes to be assured of strong repair, he may use a narrow strip of whole skin as has already been mentioned.

Fig. 1.

Fig. 2a.

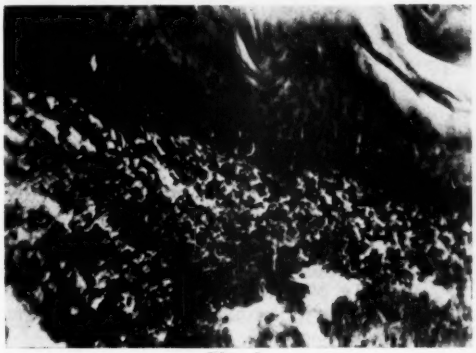

Fig. 2b.

Fig. 2c.

Fig. 1. Biopsy of a full thickness skin graft, taken approximately 2 years after the operation (Record 22.871).

Fig. 2. Full thickness skin graft which loosened a few days after the grafting. Recidivation but perfect tolerance of the grafted skin. New operation after 16 months; results of the biopsy: (Record 42.671) a, growth of exogenetic origin, surrounded by granulomatous giant cell tissue, with plasmodia of the foreign body type. b, Hypertrophic epidermis with softening of the papillary cones. The proximal dermis is infiltrated with round cells. A layer of uniform connective tissue is observed, with neopapillae containing red cells. c, Atrophic epidermis over epidermic cyst.

This is a rapid and safe procedure occupying an intermediate position between the use of a graft and the usual suture methods. In recurrent hernias, which in reality are expressions of the failure of former reconstruction, the whole thickness skin graft is strongly indicated. The value of this graft increases the weaker and more disorganized tissues found at operation, especially if there has been more than one recurrence.

Femoral hernia. Femoral hernias show little tendency to recur. Their reconstruction is easily done with the use of general techniques. Should one wish for greater security—or in case of recurrence—the skin graft used should be fixed via the inguinal ligament to Cooper's ligament as already described. In 1 case of femoral hernia with 3 recurrences and almost total destruction of the inguinal ligament, we fixed the graft via the femoral route to Cooper's ligament, displacing the vein outwardly; the upper end was fixed to the aponeurotic portion of the internal oblique and to the deep surface of the external oblique. In small femoral hernias we suture inguinal ligament to Cooper's ligament with a narrow skin strip.

Umbilical hernia. This type of hernia, especially when it appears in old and obese

Fig. 3. Removing a whole thickness skin graft. The graft is kept tense over the left forefinger, and is carefully separated from the underlying fat. Inset shows the technique of obtaining a graft to repair an inguinal hernia. Outline of the graft, *B*; elliptical inguinal incision that circumscribes the classic operating field, *A*.

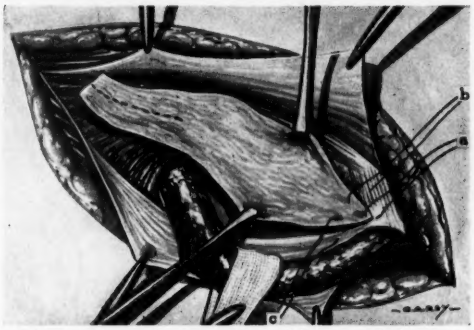

Fig. 5. The graft, maintained with two Allis forceps is fixed at its internal end. This drawing shows: *a*, the suture that includes the fibrous tissues covering the pubis; *b*, the suture that includes the lower part of the sheet of the rectus; *c*, the suture that includes the medial end of the inguinal ligament.

patients, has a great tendency to recur. The use of a whole thickness skin graft is firmly indicated in these cases. For umbilical hernias as well as for big incisional hernias, we prefer general or spinal anesthesia to obtain good relaxation of the abdominal walls.

To avoid recurrences, we endeavor to superimpose the greatest number of layers possible over the opening of the hernia; furthermore, we include a new strong element, the whole thickness skin graft.

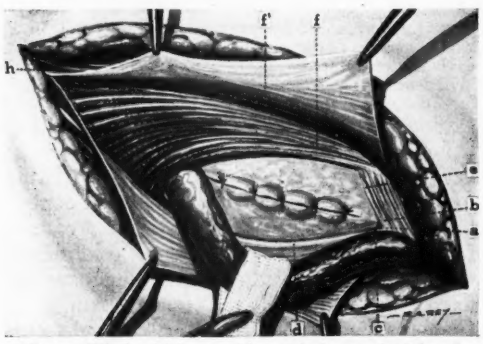

Fig. 4. Whole thickness skin graft in inguinal hernia. (The technique follows in general lines that of Mair.) This drawing shows the fascia transversalis carefully folded and stitched, in order to provide a tense bed for the graft. Future points of attachment of the graft are: *a*, fibrous tissues covering the pubis; *b*, lower part of the sheet of the rectus; *c*, medial end of the inguinal ligament; *d*, inguinal ligament; *e*, external end of the sheet of the rectus; *f*, conjoined tendon; *f*, deep aspect of the aponeurosis of the obliquus externus; *h*, obliquus externus.

Mair's reconstruction follows the Mayo technique. The skin graft is fastened over the overlapped aponeurosis. We use Araya's modification of the reconstruction methods of Quénu and Gersuny. Also the graft removed before the lipectomy (13) is interposed as follows: after the orifice of the hernia is closed vertically the separation of the rectus muscles is determined and vertical flaps are cut in the interior leaf of each sheath. These flaps are folded inward and sutured together. The rectus muscles are mobilized, separated from their sheaths and sutured at their inner borders. A bed is thus prepared to hold the graft. The graft is first fixed with 4 cardinal stitches, one above and another below in the midline, the other two on the sides, the graft being introduced under the front leaf of the sheath. Then, with the graft held tight, we fix it to the deep surface of the anterior leaf of the sheath. If possible, the excess sheath is partially sutured together with every little tension, so as not to loosen the underlying graft. In other cases we have used the technique of Neil MacLean to cover the skin graft.

In small umbilical hernias repair was done according to the Mayo technique by overlapping the wall and using as suture material a narrow skin strip. It has extra-ordinary resistance and is indeed superior to fascia strips.

If extensive lipectomy is necessary and drainage is used, we use tubes or rubber dam

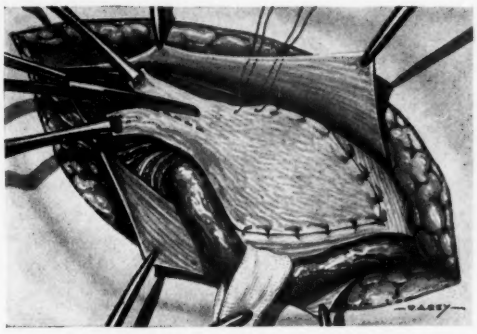

Fig. 6. Incision in external end of the graft is made to obtain two pedicles or tails.

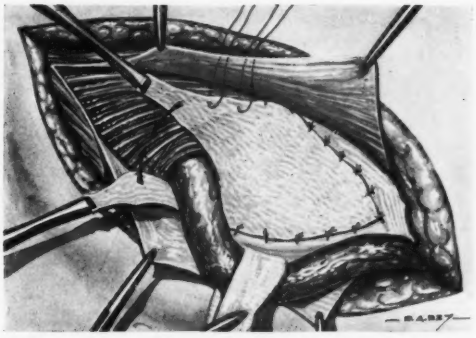

Fig. 7. The cord is passed between the two pedicles of the outer end of the graft.

sheets which do not come in contact with the graft but emerge through the angles of the incision, or better still we make a counter-opening. Drains should be left in place at least from 5 to 7 days.

Incisional hernia. Incisional hernias are an evidence that the former suture did not hold. If the opening is small, repair can be made with the usual suture procedures. If the opening is large, however, and the abdominal walls are weak, it is best to use a graft. In very large incisional hernias in which the abdominal walls cannot be pulled together a skin graft must be used as routine.

After the graft is taken and once the sac is treated (preferably by reduction and plication above, or in the presence of a very large hernia, by opening, resection and suture), the reconstruction is carried out. Considering the condition of the walls and the location of the hernia every ventral or incisional hernia presents a different problem. Nevertheless, three types may be considered briefly: the umbilical hernia, supraumbilical hernia, and lateral incisional hernia (15).

If the incisional hernia is large we make it a practice to include 2 or 3 preoperative pneumoperitoneum inflations (Goñi Moreno technique) in the preparation of the patient so as to increase the abdominal capacity and to facilitate visceral handling during operation.

In *subumbilical incisional hernias* we identify the inner borders of the rectus muscle sheaths and approximately 1 centimeter from the borders we make an incision to open the sheath. The inner flaps are mobilized and a new subumbilical midline is constructed. The sutures are placed so as to include one flap, the fundus of the ventral hernia (this step must be done with great care as the hernia is made up of peritoneum covered with remains of the transversalis fascia) and the other flap. The aponeurotic pad so formed is made tense with two distal stitches, which are fixed one to the

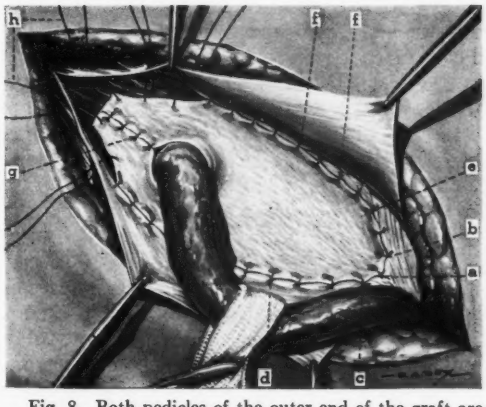

Fig. 8. Both pedicles of the outer end of the graft are joined together with stitches, *g*, taking care not to strangulate the cord, and forming an orifice through which the cord emerges well displaced outward. Attachment of the graft: *a*, the stitch that includes the fibrous tissues covering the pubic; *b*, the suture that includes the lower part of the sheet of the rectus; *c*, the suture to the medial end of the inguinal ligament; *d*, sutures anchoring the graft to the inguinal ligament; *e*, sutures to the external edge of the sheet of the rectus; *f*, suture to the conjoined tendon; *f*, suture to the conjoined tendon and to the deep aspect of the aponeurosis of the obliquus externus; *g*, stitches uniting both pedicles of the graft; *h*, stitches giving tension to the external end of the graft.

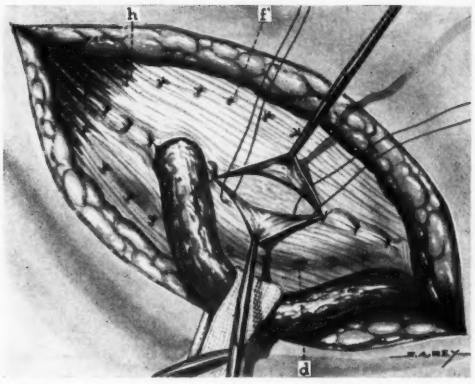

Fig. 9. The aponeurosis of the external oblique is laid over the graft and sutured loosely. Should the edges of the aponeurosis not join properly, they are only partially sutured. The cord, as a result of the retrofunicular reconstruction remains subcutaneous.

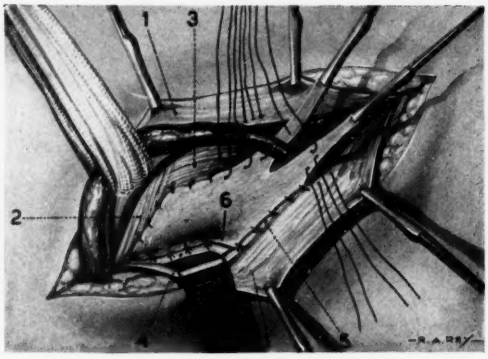

Fig. 10. In cases where inguinal ligament is naturally weak, or has been artificially weakened by previous operations, the graft is fastened by its lower border to Cooper's ligament. *1*, Obliquus externus; *2*, rectus sheet; *3*, conjoined tendon; *4*, Cooper's ligament; *5*, inguinal ligament; *6*, graft passing over the femoral vein.

anterior leaf of the sheath near the umbilicus, and the other, the inferior, to the lower part of what remains of the midline or to the superior border of the pubis. The rectus muscles are then mobilized and approximated at their inner borders. The graft, which has already been trimmed to size and shape, is applied to the muscles by its deep surface and is fixed to the periphery of the aponeurotic opening of the sheath.

In cases of *supraumbilical incisional hernias* we repair the hernia with a technique similar to that described for umbilical hernia.

In *lateral incisional hernias* the technique is usually more complicated. We try to obtain a superficial aponeurotic layer and a deep muscular layer. Once the layers are separated and mobilized, the muscular borders are sutured together (Fig. 11 a, b, c). Then the graft is placed on, and fixed to, the deep surface of the aponeurosis. The excess of aponeurosis is folded over and sutured as well as possible with care not to loosen the underlying graft. If this is not possible there are other ways of fixing the whole thickness skin graft not so perfect but nearly as good as the technique mentioned before (Fig. 12 a, b, c, d).

CASE HISTORIES AND DISCUSSION

We shall report here the results obtained in repairing 211 hernias with whole thickness skin grafts. The patients were treated over a period of 3½ years—from May, 1946 through November, 1949.

The total number of cases was 225, but as 14 of the patients (8 inguinal and 6 with incisional hernias) were operated upon in private clinics by some of our associates and the clinical histories are incomplete, they are not suitable for statistical purposes and have been omitted. Thus the final number of patients becomes 211.

In order to arrive at statistical conclusions, we transferred the clinical histories to large tables divided into columns, showing general data such as sex, age, type of hernia—if recurrent the character of the former operation, time elapsed until recurrence, length of time until reoperation was done; type of operation with technique used, anesthesia, surgeon, surgical findings, reasons for use of graft; early postoperative course, including antibiotics used, time the patient was kept in bed, complications; and follow-up with results and observations. Only the more important findings will be included in this report.

The patients were operated upon by Dr. Ricardo Finochietto, our associates, and ourselves: 122 cases in the Municipal Postgraduate Surgical School (Rawson Hospital, Buenos Aires) and 89 in private clinics (see Table I). In all the patients we were able to follow

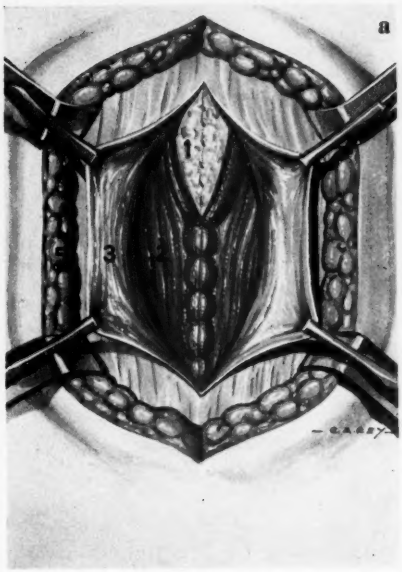

Fig. 11a.

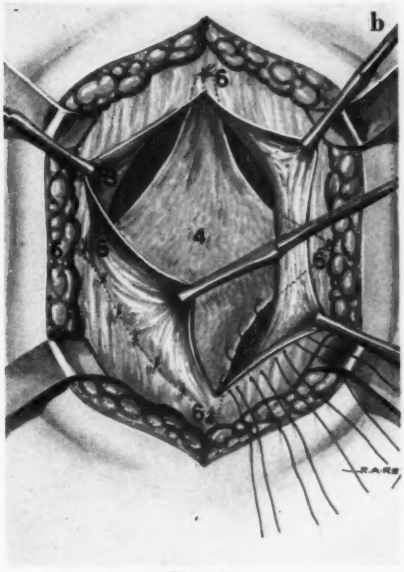

Fig. 11b.

the early postoperative course and the complications. As to the late postoperative course it was easy to follow in the patients operated upon in private clinics, as the patients were always in touch with their surgeons. In the patients operated upon in the hospital we could follow only about 55 per cent. To overcome this difficulty we inquired of colleagues who work in other hospitals of this city as to the results and they report that they have observed no recurrences in the patients of this series who were treated with whole thickness grafts.

The total number of cases included 135 inguinal hernias of which 87 were primary and 48 recurrences, 4 femoral hernias, 21 umbilical, and 51 incisional hernias.

Among the most important complications (Table II) were 5 cases of suppuration (2.36 per cent); recurrence in an inguinal hernia, 2 cases in which the graft was not tolerated, and 2 "false recurrences" the result of weakness of the walls in a zone distant from the graft, that is to say the recurrences were not due to failure of the graft.

We shall now discuss the results for each type of hernia.

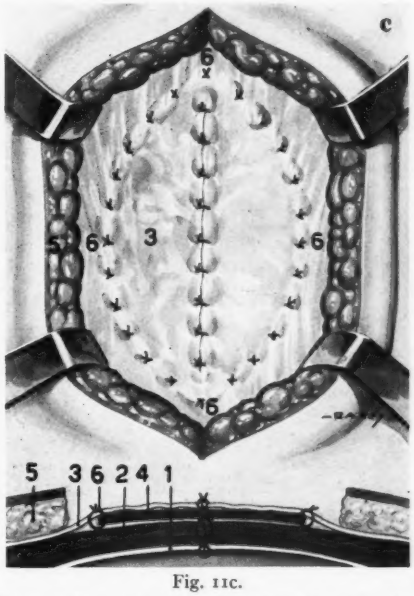

Fig. 11c.

Fig. 11. Reconstruction of incisional hernia graft laid on muscular bed and completely covered by aponeurosis. a, Preparing the muscular layer; b, attachment of graft to deep aspect of aponeurosis; c, graft completely covered by aponeurosis. *1*, peritoneum and properitoneal fat; *2*, muscle; *3*, aponeurosis; *4*, graft; *5*, skin and fat.

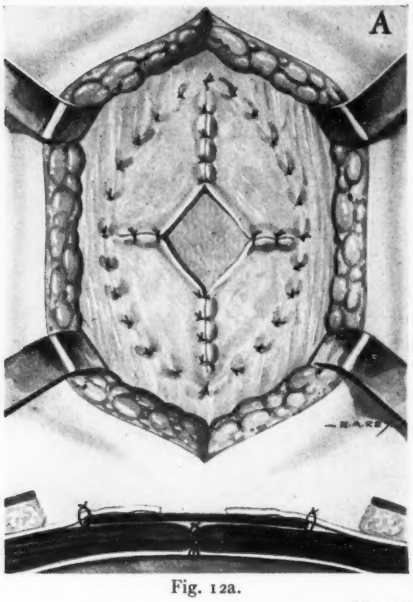

Fig. 12a.

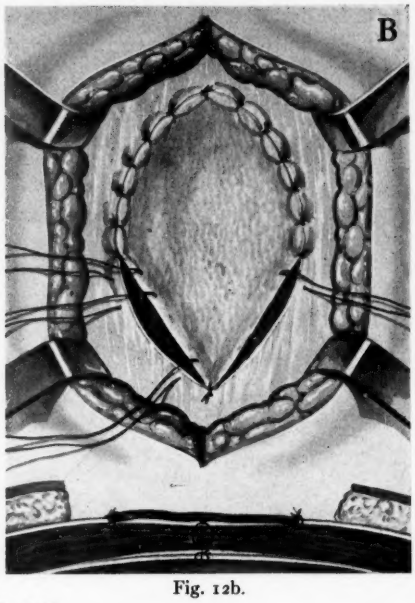

Fig. 12b.

(*Legend on opposite page*)

Inguinal hernias. In the Municipal Postgraduate Surgical School 78 inguinal hernias were repaired with whole thickness skin grafts between May, 1946 and November, 1949. To this number should be added 57 hernias operated upon in private clinics by the same surgeons who work in the Municipal Postgraduate Surgical School. Of these 135 inguinal hernias repaired with whole thickness skin grafts, 10 were operated upon in 1946, 31 in 1947, 44 in 1948, and 50 in 1949. With the use of whole thickness skin we abandoned definitely the use of "fascia lata propria" the graft we preferred before using the skin. Preserved "bovine fascia" was used less often; however, in some selected cases we still use these strips. Eighty-seven of the 135 inguinal hernias were primary and 48 recurrent. Of the primary hernias 66 were indirect, 17 were direct, and 4 were direct-indirect hernias. Local anesthesia

TABLE I.—DISTRIBUTION OF CASES

	1946*			1947			1948			1949†			Total		
	H.C.	P.C.	Total	H.C.	P.C.	Total	H.C.	P.C.	Total	H.C.	P.C.	Total	H.C.	P.C.	Total
Inguinal, primary	5	1	6	10	8	18	13	16	29	22	12	34	50	37	87
Inguinal, recurrent	3	1	4	9	4	13	8	7	15	8	8	16	28	20	48
Inguinal, total	8	2	10	19	12	31	21	23	44	30	20	50	78	57	135
Femoral								1	1	3		3	3	1	4
Umbilical				6		6	1	4	5	4	6	10	11	10	21
Incisional	5	1	6	4	4	8	10	6	16	11	10	21	30	21	51
Total	13	3	16	29	16	45	32	34	66	48	36	94	122	89	211

*Since May.
†Until November (period of three years and six months).
H.C. Hospital cases (Municipal Post-Graduate Surgical School, Rawson Hospital, Buenos Aires).
P.C. Private cases.

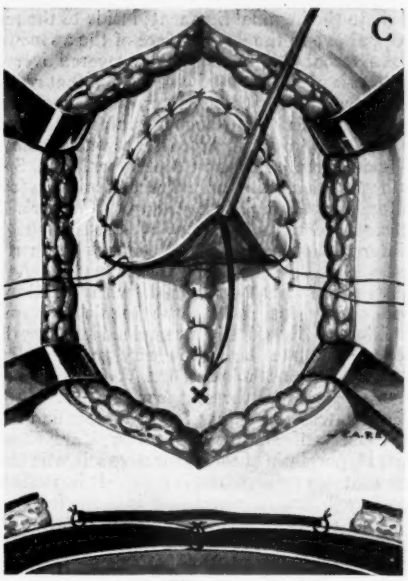

Fig. 12c.

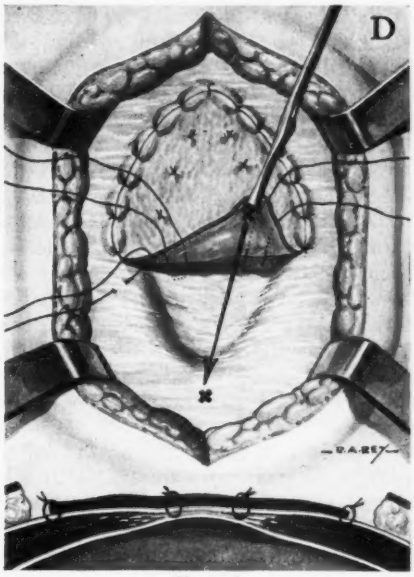

Fig. 12d.

Fig. 12. Other possibilities of fixing the graft in incisional hernias, not so perfect but nearly as effective as the preceding one. a, Graft laid on the muscle and partially covered by the aponeurosis. b, Graft laid on the muscle and fixed to the aponeurotic border. a, All the layers have been sutured together. The graft is attached to the aponeurosis covering the suture. d, The borders of the incisional hernia cannot be brought together. The graft, fixed to the aponeurosis, closes the gap.

was used in 73 cases, general in 3, and spinal in 11 cases. Sixty-one were treated by fixing the graft below to the inguinal ligament, and in 13 the graft was fixed to Cooper's ligament. Thirteen hernias which presented less anatomical alterations were sutured with a narrow strip of whole skin.

The main reason for the use of a skin graft is the weakness of the walls, especially of the conjoined tendon, causing thus a large Hessert's triangle. Another important reason is the disorganization and expansion of the deep inguinal ring caused by the voluminous neck of a sliding hernia. Five hernias of this kind were operated upon. The technique was briefly this: preoperative pneumoperitoneum to increase the abdominal capacity; LaRoque's maneuver to reduce and treat the sac if it was a case of ileopelvic sliding—if a cecal sliding, Zimmerman's or Bevan's technique; transposal of cord with Schmieden's technique and application of a whole thickness skin graft, preferably sutured to Cooper's ligament.

TABLE II.—COMPLICATIONS

Complications	Ing.	Fem.	Umb.	Incis.	Total
Local—early					
Wound sepsis	1		2	2	5
Serous discharge	1			1	2
Hematoma, scrotum	3				3
Hematoma, wound	2		1	1	4
Wound disruption				1†	1
Mild tumefaction, cord and testis	12				12
Local—late					
Graft intolerance	2*				2
Recurrence	1				1
"False recurrence"			1	1	2
General					
Thrombophlebitis	3¶				3
Postop. dyspnea				1	1
Intestinal distention				1†	1
Lung atelectasis			1‡		1
Shock				1	1

*One clear and one dubious.
†Associated complication of intestinal distention and wound disruption.
‡Associated with wound sepsis.
¶In 1 case, ligature of superficial femoral veins. In 2 cases, medical treatment. All cured.

Of the 48 *recurrent hernias*, 32 were first recurrences, 15 were second recurrences, and 1 was a third recurrence. For us, a recurrence, which is an expression of failure of the usual suture employed in the previous operation or operations, is sufficient justification for the use of a whole thickness skin graft. This opinion is strengthened by the number of hernias that recur more than once, and also by the fact that the anatomical elements which had been used in the reconstruction were found to be weak. Of the 48 recurrent hernias, 37 were indirect, 10 direct, and in 1 case we found a pantaloon or direct-indirect hernia. In 42 cases local anesthesia was used, 3 had general and 3 had continuous spinal anesthesia by means of a catheter.

In 1 patient of the group of 135 inguinal hernias, 0.74 per cent, treated with whole thickness skin graft, the graft suppurated. Mair gives a 3.3 per cent incidence of infection for 149 inguinal hernias, and Marsden notes 10 cases of moderate infection in 163 operations.

Following is a brief report of a case.

No. 36,893. R. A., 46 year old male, was operated upon for a right scrotal hernia on January 31, 1947. Local anesthesia was used. A whole thickness skin graft was fixed to the inguinal ligament, rectus sheath, and conjoined tendon, and covered with the external oblique. After operation penicillin therapy was administered. On the 5th day a phlegmon appeared in the wound. After the stitches were removed great suppuration appeared. Pieces of aponeurosis were progressively eliminated but the graft remained in good condition. Two months later, the granulations were covering the graft. One month afterward the wound was healed. The graft was perfectly tolerated.

In one of our cases there was a recurrence. Mair gives 1 recurrence in 87 cases; Marsden reports a higher figure, namely, 9.8 in 136 operations.

No. 42,671. R.F., male, 24 years of age, 5 years ago was operated upon for acute appendicitis and drainage was applied. A large fibrous scar persisted in the iliac fossa. Three years ago he was operated upon for inguinal hernia of the right side; recurrence followed 1 month after operation, and patient was operated upon in June, 1948, under local anesthesia. A large direct sac that extended across the internal transversal oblique was resected and the deep layer plicated. A whole thickness skin graft was placed and fixed as follows: below to Cooper's ligament, outside to the inguinal ligament; inside to the rectus sheath, above to the deep surface of the aponeurosis of the external oblique and finally covered over with aponeurosis of the external oblique. Patient rested in bed for 1 week. Twenty days later, on making an effort he felt that "something became unfastened" in the wound; shortly afterward recurrence was visible. He was again operated upon in September, 1949. Spinal anesthesia was used. A large direct hernia was found. The former graft had loosened from Cooper's ligament and had the appearance of fibrous tissue over the internal oblique muscle. A biopsy specimen was taken and sebaceous material was noted. A new reconstruction was performed with fixation to Cooper's ligament and to the inguinal ligament. Penicillin was given. Patient remained in bed 15 days. Three months later he was in very good condition.

Report of the pathologist, Dr. V. Iaricci: "In the sections of the tissue there appear (Fig. 1): skin with epidermic atrophy, mainly in the malpighian layer; basal conserved. Dermis with no papillae. Elastorrhexis. Hyperplasia of the connective sclerotic tissue, which contains two epidermic cysts. It is possible to observe well limited zones and isolated from each other, one of them juxtacystic with gigantic granulomatosis cells. Many fragments were found, probably suture threads some of them intracellular. In the deep dermis it is possible to see a layer of connective collagenous and fibrous tissue containing numerous newly formed capillaries enlarged and full of red cells. Diagnosis: "Epidermic atrophy. Elastorrhexis. Gigantoblastic granulomatosis. Sclerosis of the deep dermis. Implantation cysts."

We want to emphasize the fact that in the combined statistics of the various authors as compiled by Mair, the number of recurrences in indirect hernias treated with the Bassini method is 11.8 per cent and in direct hernias 16.8 per cent. In the patients treated with fascia strips the figures are 6.75 per cent and 5.6 per cent, respectively.

In 1 case of simultaneous bilateral operation, one of the grafts was not tolerated. It was necessary to operate again in order to remove it, but the underlying fibrosis was sufficiently strong to maintain, up to the present, a good wall.

No. 38,102. M.A., a 27 year old male, was operated upon for bilateral inguinal hernia, in June, 1947. A whole thickness skin graft was set and fixed to both sides of the inguinal ligament. The wound healed by first intention and the grafts were perfectly tolerated until March, 1949, that is for nearly 2 years. At this time a slightly painful tumefaction appeared in the right side. A cloudy liquid was withdrawn and sulfanilamide was injected. As the inflammation appeared once more it was evident that the skin graft was not tolerated. Reoperation

was performed in May, 1949. The cutaneous sheet, which was firmly fixed to the neighboring tissue, was completely removed. Over this, there was a cavity which contained a cloudy liquid and in one of the stitches that was placed through the inguinal ligament there was a small granuloma which caused the intolerance. After the graft was removed the wound healed quickly and the hernia has not recurred up to this time.

The pathologist's report on the piece of skin removed, states: "Histologically the material pertains to skin with epidermic atrophy, which covers a sclerified corium, with nearly a total disappearance of the adnexa, and infiltrated by a slight number of lymphocytes and plasma cells. Toward the borders, the epidermis loses its superficial layers and the basal one is the only one that remains. The corium is full of lymphocytes; there is also a regular amount of newly formed blood vessels."

Another patient 3 months after operation and after a normal postoperative course, presented a puriform discharge from the wound. This patient did not come back to our service. He was treated in another hospital where the graft was removed. We have no other information regarding this case and we have included it, though dubiously, among the "graft intolerances."

In 3 cases hematomas of the scrotum appeared (2.2 per cent). It was necessary to open one of them. Mair records 3.3 per cent in his series.

Temporary tumefaction of the wound is frequent. It appears in 20 to 30 per cent of the cases; it is caused by the disintegration of the epidermic layers of the graft. In 2 cases this tumefaction was so great that the possibility of infection was considered and the wound was partially opened; only a small quantity of nonpurulent cloudy liquid oozed, and with penicillin therapy the complication was overcome.

Temporary tumefaction of the cord and the testicle appeared in approximately 10 per cent of the cases; it subsided with the usual therapy-rest, use of a suspensory bandage, ice bag.

When we use a skin graft, we prefer not to perform an appendectomy at the same time. Nevertheless we did so in 5 cases and no complications arose.

The use of whole thickness skin grafts in strangulated hernias, with no previous preparation and with the possiblity of contamination which apparently could prove dangerous, was successful in our experience. Thus such a supposition was invalidated. Six cases of strangulated hernias were treated with whole thickness skin grafts and healing was perfect: 4 inguinal, 1 incisional, and 1 femoral hernia with mortification of the bowels compelled the surgeon, Dr. Chouhy, to perform resection and enteroanastomosis.

Femoral hernia. We have had opportunity of using whole thickness skin grafts in 4 cases of femoral hernia. One was a voluminous femoral hernia that had recurred three times. As the patient had had repeated bouts with erysipelas in the groin, in a preliminary operation the skin of that zone was resected. In a second operation reconstruction was done with a whole thickness skin graft taken from the thigh. No inguinal ligament was found, so the graft was fixed to Cooper's ligament and surrounding fibrous tissues. The result was perfect. Another recurrent and strangulated hernia has already been mentioned. In 2 small primary femoral hernias, a narrow skin strip was used to suture the inguinal ligament to Cooper's ligament. We have included in the list of inguinal hernias 2 cases of inguinal hernia which were associated with a femoral sac. Both patients were treated via the inguinal route with skin grafts fixed to Cooper's ligament.

Umbilical hernia. We have treated with whole thickness skin grafts 11 umbilical hernias in the hospital and 10 in private clinics. Nineteen were primary hernias and 2 were recurrences. Seventeen were large umbilical hernias and 4 were of minor size. The reconstruction was done in 15 cases by preparing the two vertical flaps of the anterior rectus sheath and suturing in the midline the edges of both flaps, suturing in the midline the edges of both recti and fixing the graft to the anterior leaf of the sheath. In 2 cases we used the Neil MacLean technique to which we added the deep interposition of a whole thickness skin graft. In the 4 smaller hernias the reconstruction was made with the Mayo overlapping technique, suturing with narrow strips of whole skin. Fifteen patients were operated upon with local anesthesia, 1 with general, 4 with simple spinal, and 1 with continuous spinal with catheter. Nine days was the aver-

age time patients were kept in bed. In 2 cases there was suppuration.

No. 40,563. R.S.F., a 66 year old male, very fat, had an umbilical hernia 8 by 6 centimeters, of 25 years' standing. He was operated upon in November, 1947, under spinal anesthesia. The reconstruction was done by fixing the graft to the rectus sheath. Penicillin therapy was administered. The postoperative course was complicated by cardiac arrhythmia and lung atelectasis. Five days later in the presence of intense suppuration, the superficial layers of the wound completely opened. The graft maintained its vitality in spite of the suppuration. Two months afterward there was complete healing. Late result was perfect.

J.F. deM., female, aged 53 years, a private case, was operated upon in April, 1949, under local anesthesia. Fixation of the graft was carried out and penicillin was given. Drainage was maintained for 3 days. On the 7th day the wound opened and a seropurulent discharge drained. The wound continued to drain abundantly for 25 days, then closed. Patient was seen in December, 1949, and was found to be in perfect condition.

We are of the opinion that the use of whole thickness skin grafts in umbilical hernias, especially in aged and obese patients, is justified due to the frequent recurrences in patients operated upon with the usual methods. With this graft we have had no recurrences, although in 1 case we could observe a slight weakness near the reconstructed zone due to the separation of the rectus. We have classified this case as a "false recurrence."

Incisional hernia. We have treated 51 patients with incisional hernias, 30 in the hospital and 21 in private clinics. Six patients were operated upon in 1946, 8 in 1947, 16 in 1948, and 21 in 1949. Of the total number, 24 were supraumbilical—midline and paramedian—16 subumbilical; 10 lateral—these generally occurred after appendectomy. There was also a lumbar incisional hernia following nephrectomy. Forty were primary hernias, 10 had recurred once, and 1 twice. Thirty-four were in women and 17 in men. Eighteen were operated upon with local anesthesia, 15 with general, 10 with simple spinal anesthesia and 8 with continuous spinal anesthesia with catheter. Three small incisional hernias were treated with a narrow strip of whole skin. In the 48 other cases we used a skin patch. Sometimes it was possible to reconstruct a deep muscular layer were we could apply the graft that was sutured to the aponeurosis. In 13 cases it was possible to cover it completely with the aponeurosis, in 26 cases this covering was incomplete. In 9 cases we fixed the graft directly to the aponeurosis. In nearly all cases drainage was accomplished by counteropening during 5 to 7 days. A thick, dark cloudy fluid, containing leucocytes but no bacteria (*vide supra*) was discharged. In 2 cases the drains were removed too soon and hematomas were formed and became infected.

No. 44,059. R.N.P., female, aged 46 years, was operated upon in September, 1947, for choledocholithiasis. The wound suppurated and an incisional hernia formed for which the patient was operated upon in January, 1948. Ten days afterward there was subcutaneous wound disruption and a voluminous right lateral supraumbilical hernia appeared. An orifice of 10 by 12 centimeters was palpable. Operation in December, 1948, under spinal anesthesia, consisted of liberation and suture of the rectus muscle and a large skin graft was applied against the muscle and fixed to the edges of the aponeurosis. Drainage applied. Penicillin was given after operation and on the 5th day the drains were removed. A blood collection formed and was emptied; it formed again and finally suppuration occurred on the 20th day. The skin graft could be seen amidst the suppuration. Four months afterward, suppuration continued. The wound was fully opened so that the healthy aspect of the graft could be seen. Peripheral counteropenings were made. Granulation increased and 3 months later the wound was completely healed. A year after operation the patient was in perfect condition.

No. 39,515. M.E.G., a 59 year old female. Five years ago she was operated upon for uterine myomas. Five months afterward the incisional hernia began. Actually it was gigantic. Five preoperative pneumoperitoneum inflations were given. Operation was performed in November, 1947, under continuous spinal anesthesia with catheter, and consisted in opening of the sheaths, approximation of the rectus and application of the graft fixing it to the sheath; drainage. The drains were withdrawn 3 days afterward. A few days later a continuous suppuration appeared. The graft remained intact and 2 months later healing was complete.

One patient sustained a wound disruption a few days after the operation.

No. 45,621. P.L.C., a 49 year old female, obese, had an incisional hernia that stretched from the pubis to the umbilicus. Operation was performed in June, 1949, under general anesthesia. The reconstruction was done in 4 layers with interposition of a whole thickness skin graft. After operation vomiting and distention appeared but became better after the

use of an indwelling intestinal tube. Distention and vomiting reappeared after patient withdrew the catheter. Six days after operation reddish serous discharge appeared. Disruption was suspected, the wound reopened and a subcutaneous wound disruption was found. Immediate operation was performed under pentothal and local anesthesia. The graft was removed and found to be unfastened at one side. Suture was done in one layer with stainless steel wire. Suppuration of the wound occurred. Patient continues in treatment.

We have not observed a real recurrence in this series; but in a big incisional hernia after a nephrectomy where a large graft was placed from the lumbar muscles to a point near the rectus, we were able to verify, 5 months after operation, a zone of weakness of the walls between the anterior end of the graft and the lateral edge of the rectus. We shall strengthen this zone with another graft. We classify this case as a "false recurrence" as the weakness appears in a place which is distant from the grafted zone.

SUMMARY

1. A study based on 211 inguinal, umbilical, femoral, and incisional hernias treated with whole thickness skin grafts, over a period of 3½ years, is presented.

2. The basic principles of this graft are discussed and it is demonstrated that the graft is harmless and that it has extraordinary resistance.

3. The general technique to obtain the skin graft is described. Emphasis is placed on the selection of sound skin, proper preparation, and careful elimination of all remnants of fat. The operation must be delicately conducted; the graft must be tautly fixed in order to obtain atrophy of the epidermic layer, sweat and sebaceous glands; the graft should be applied preferably to a muscular bed, sutured to the aponeurosis or fibrous tissues and covered with aponeurosis if possible, if not, it is also well tolerated covered with subcutaneous tissue. Only 5 cases, 2.36 per cent, of infection of the graft was observed: 1 recurrence, 2 "false recurrences," and 2 cases of remote intolerance.

4. The special technique used in cases of inguinal, femoral, umbilical and incisional hernias is described.

5. Of 135 inguinal hernias, 87 were primary, 48 recurrent; 1 suppurated and in 2 the grafts were not tolerated.

6. Of 4 femoral hernias, in 2 a skin patch and in 2 a narrow strip of whole skin were used. No complications were observed.

7. In the group of 21 umbilical hernias, 1 suppurated but did not recur and in 1 a "false recurrence" was found.

8. Of the 51 cases of incisional hernias, there were 24 supraumbilical, 16 subumbilical, 10 lateral, and 1 lumbar. In 2 cases suppuration occurred but the graft was tolerated and no recurrences were found. There was 1 wound disruption in the early postoperative course and 1 was a "false recurrence" due to weakness of the wall distant from the zone where the graft was applied.

9. The 6 patients in the strangulated hernia group were operated upon as emergencies—4 inguinal, 1 femoral, and 1 incisional hernia. Repair was done with whole thickness skin grafts. All healed without complications.

10. Comparing our results with those obtained with plain reconstruction strips or patches of "fascia lata propria" and preserved "fascia bovis" strips (a technique used largely before 1946), it was found that the use of whole thickness skin grafts has many advantages, among which are the simplicity of the technique, the fact that the grafts are obtained from the zone of operation, the reconstructed area is strong, and the incidence of complications low. It is the opinion of the authors that the whole thickness skin graft at the present time is the method of choice whenever a graft is needed to repair a hernia or when it is desired to assure against a recurrence.

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INTUSSUSCEPTION IN INFANCY AND CHILDHOOD

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INASMUCH as intussusception is one of the most common surgical conditions encountered in infancy and childhood, it seemed appropriate to review the large number of cases encountered at Children's Hospital, Washington, D.C. During the years 1940 to 1947, inclusive, 65 proved cases of intussusception were encountered. In addition there were 12 suspected cases in which confirmation at the time of laparotomy was lacking and in some of which spontaneous reduction of the intussusception had undoubtedly occurred. These latter cases were omitted from this series.

GENERAL CONSIDERATIONS

During this period, the total number of admissions to Children's Hospital was 51,469, which represents an incidence of 0.12 per cent of intussusception. The ratio of white to colored patients was roughly proportional to the ratio of white and colored admissions. Intussusception was encountered in approximately twice as many males as females. The average age of the patient in this series was 13 months, the range being from 3 weeks to 6 years. Only 3 patients were over 36 months, while in only 4 cases was the child younger than 3 months.

ETIOLOGY

Many theories have been proposed to explain the pathogenesis of intussusception and many etiologic factors have been identified in isolated cases. However, no single etiologic factor can explain any large number of these cases, and this problem excited our interest and study. Significant features of probable etiologic significance in this series included diarrhea, 3 cases; polyps of the ileum, 3 cases; Meckel's diverticulum, 1 case; Meckel's diverticulum with diarrhea, 1 case; and diarrhea plus an ileal polyp, 1 case. However, the one striking finding was the presence of enlarged ileocecal lymph glands in 14 of the 65 cases. It has been our observation in personally observed cases that the occurrence of enlarged ileocecal lymph nodes is a rather consistent finding in intussusception, more often present than operative records indicate. The significance of this lymphadenopathy has often been discounted, being interpreted as a consequence rather than a cause of the telescoping of the bowel. This explanation, however, would seem to be contradicted by the fact that the lymphadenopathy observed by the authors is usually confined to the ileocecal region, whereas the lymph glands of other intussuscepted segments of the small and large bowel are rarely enlarged. Furthermore, conspicuously enlarged nodes have been frequently observed when the intussusception has been of minimal duration. As Perrin and Lindsay have pointed out, similar hyperplasia of the relatively large amounts of lymphoid tissue present in the terminal ileum and in the ileocecal valve at this age may be of etiologic importance.

PATHOLOGIC FINDINGS

The incidence of the various types of intussusception in this series coincides with reports of other large series (2, 3, 6, 7). The majority were of the ileocecal, 37 cases, and ileocolic, 17 cases, types, while the enteric, 9 cases, and colic, 2 cases, occur less frequently. Retrograde intussusception, occurring as a part of double intussusception, was noted in 1 case. It may be said at this point that agonal intussusceptions, which are so frequently seen, have been meticulously excluded from this series, since we feel they are of no clinical importance.

The pathologic changes in the intussuscepted bowel depend largely upon the duration of the intussusception plus the security and firmness with which the intussusceptum is held. The size of the lumen of the intussus-

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cipiens is also an important factor in determining the extent of damage. All degrees of intussusception were encountered in this series, varying from a loose telescoping in which the intussuscepted bowel was readily reduced and exhibited no discernible pathologic change, to those cases with advanced gangrene of the intussuscepted segment in which reduction was impossible. The extent of damage to the intussuscepted bowel depends largely on the edema that develops, causing an encroachment on the mesenteric vessels. The initial disturbance involves the veins of the torsed mesentery, causing vascular engorgement and swelling of the intussuscepted bowel and, after a variable length of time, compression of the arteries follows. Obviously the narrow caliber of the small bowel leads to earlier vascular damage than when the larger, more distensible colon forms the intussuscipiens. The duration of the intussusception is of extreme importance in determining the extent of pathologic change and final gangrene.

SIGNS AND SYMPTOMS

In 15 cases, a history of recent upper respiratory infection was elicited, and in our opinion this represents a significant sequence of symptoms inasmuch as mesenteric adenitis, so often associated with respiratory infections, may play an important etiologic role in these cases.

A history of paroxysmal abdominal pain, mild shock, and blood-stained rectal discharge is characteristic and tantamount to a diagnosis. The onset of intussusception is usually sudden and terrifying to both mother and infant. It strikes without warning a previously healthy, robust infant. The initial symptom is pain of such severity that the victim screams violently and soon appears mildly shocked. The pain is paroxysmal in character and the child usually appears comfortable in the interim. These agonizing paroxysms of pain with apparent well-being in the intervals is of great diagnostic value. In all but 3 of our cases this pain pattern occurred. A similar incidence of pain has been observed by other authors (2, 4, 7).

Vomiting, an important symptom, is usually frequent and copious. In our series, it was noted in 59 of 65 cases, was absent in 3, and was not mentioned in an additional 3. Similar statistics are found in the literature, its occurrence being noted in 100 per cent of Harkin's cases.

The character of the stools should be carefully observed. As the result of bleeding into the bowel, the infant passes stools which may be bloody, "currant jelly," or "tarry" in appearance. Presence of such a stool in an infant or young child should immediately suggest the diagnosis of intussusception. Since this may not occur for 24 to 48 hours, every effort should be made to establish the diagnosis without awaiting its appearance. In our cases, blood in the feces or on the examining finger was noted in 48 instances; it was absent in 14; and its presence or absence was not noted in 3. We were unable to establish a correlation between the duration of symptoms and the onset of bloody or tarry stools.

PHYSICAL FINDINGS

Aside from recognition of mild shock, dehydration, and acidosis, the pertinent physical findings are confined to the abdomen and rectum. Abdominal tenderness is not as prominent a symptom as one might expect, being noted in only 20 cases. Rigidity of the abdominal wall is less frequent, occurring in 10 cases. Its presence is, however, a poor prognostic sign inasmuch as 3 fatalities occurred in the 10 cases in which it was present.

A palpable abdominal mass is the one most important physical finding. It is usually felt without difficulty because of the absence of abdominal rigidity and tenderness. Coincident with a paroxysm of pain, the mass grows hard and is usually tender, while between paroxysms it is, interestingly enough, nontender.

Since the abdominal mass is usually palpable within 12 hours of onset of symptoms, it will probably be noted before rectal bleeding occurs. It may be palpated anywhere in the abdominal cavity. If the mass lies under the costal margin, its palpation may be difficult. Change in position of the mass over a period of several hours is an important sign and indicates progression of the intussusception along the course of the colon. The location of the

TABLE I.—MORTALITY AS INFLUENCED BY DURATION OF SYMPTOMS

Author's series				Mortality of other authors					
Duration of symptoms—hrs.	Cases	Died	Mortality %	Ladd and Gross %	Mussil %	Oberhelman %	Magney %	Hogg and Donovan %	Gross and Ware %
0 to 24	30	1	3.3	0	0	2.3	18	4	0
24 to 48	19	4	21	21	26	16	23	20	11
48 to 72	12	3	25	28	32	40	50	40	15
72 to 96	4	3	75	38		50		80	15

abdominal mass in this series was noteworthy in that it was palpated in either the right or left upper abdomen in 72 per cent of the cases. As the intussusceptum proceeds along the colon, it may finally protrude through the anus. More commonly it may be felt on rectal examination. A rectal or low sigmoidal mass was identified by digital examination in 8 of our cases or 12 per cent. In one of these the mass was literally protruding from the anus. It was observed that the advanced location of the intussusception was associated with a 50 per cent mortality. Furthermore, it was evident that no definite time interval is required for the intussusceptum to reach the rectum, the shortest interval being 8 hours and the longest 76 hours. However, in spite of the advanced progress of the intussusceptum, the viability of the bowel is rarely jeopardized before 24 hours.

DIAGNOSIS

The establishment of an early diagnosis is all-important in avoiding irreparable damage of the intussuscepted bowel. Irreducibility of the intussusception and gangrene of the involved bowel increase in direct ratio to the hours of intussusception. In our cases, the average duration of symptoms was 23 hours, varying from 3 hours to 76 hours. The danger of failure to establish an early diagnosis is well demonstrated by the contrasting mortality rates in early and late cases, an observation noted in other reports (Table I). The average time interval between hospital admission and surgery was 4 hours, this period being devoted to the completion of confirmatory diagnostic studies, replacement of fluids, etc. However, in 2 cases a delay of 12 hours and 48 hours respectively before surgery was associated with irreversible damage to the bowel, with subsequent fatal outcome.

X-ray examination of the abdomen was infrequently resorted to; it was employed in 10 cases. Although roentgenologic examination by means of a flat plate of the abdomen or a barium enema may contribute to the diagnosis in isolated cases, it is felt that this aid is seldom required. The flat plate may reveal evidence of small bowel obstruction with or without demonstrable fluid levels, while barium enema studies may demonstrate an obstruction at the site of the caput of the intussusceptum. In several cases which were not included in this series, it was demonstrated that the employment of barium enema resulted in a reduction of an intussusception. However, these roentgenologic studies in the average case consume time to the detriment of the child's welfare.

Leucocytosis was present in 13 cases, in 4 of which gangrene had supervened and resection was necessary. A leucocyte count over 10,000 per cubic millimeter indicates advanced damage of the involved bowel.

The temperature may range from subnormal to 106 degrees F. In 19 cases, in which the rectal temperature was 101 degrees or above, there were 6 fatalities, indicating that a marked elevation of temperature is of serious prognostic significance.

TREATMENT

It is our firm conviction that intussusception, once diagnosed, requires immediate operative correction. Our experience with the nonoperative reduction of the intussusception by means of the hydrostatic pressure of a barium enema has only served to impress us with its shortcomings. The objections to such treatment include lack of complete certainty

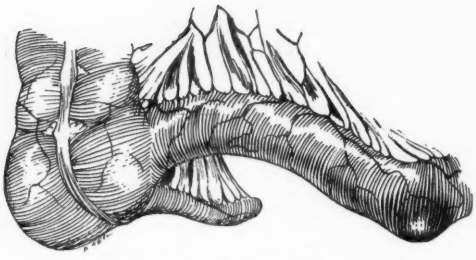

Fig. 1. Localized area of edema and hemorrhage of the terminal ileum.

that reduction has been effected, the reduction of an irreparably damaged bowel with subsequent perforation and peritonitis, failure to recognize an attendant etiologic lesion, such as a Meckel's diverticulum, and finally, the involved waste of precious hours in those cases subsequently requiring surgical reduction.

Since these infants are often in mild to moderate shock, adequate preoperative preparation is essential to the success of the subsequent operative procedure. If the duration of the intussusception has been less than 24 hours, disturbances of fluid and electrolyte balance are not marked and are readily corrected by the subcutaneous or intravenous use of 5 per cent glucose in Hartmann's solution in amounts of 150 to 500 cubic centimeters. Blood transfusions are reserved for those in whom the duration of the condition has exceeded 24 hours or in whom shock is prominent. In the event that any substantial amount of food or liquids has been ingested in the preceding 4 hours, gastric lavage is indicated preoperatively.

The proper choice of an incision is of paramount importance. One is not infrequently tempted to place an incision over the site of the palpable mass, which may be on the left side of the abdomen. However, since the final and most difficult part of the reduction is almost invariably in the region of the cecum, an incision placed in this vicinity is desirable. Such an incision may be vertical or transverse.

After location of the head of the intussusceptum, reduction was readily accomplished in the majority of cases by gently squeezing the head of the intussusceptum in an orad direction. This may be combined with gentle traction on the intussuscepted bowel, but this pulling should never be as great as the force directed against the distal portion. Contrary to the experience of others (3, 6), the location of the mass gave no index as to the viability of the involved bowel. The belief that the more anad the mass, the more often was gangrene of the intestine present did not obtain in this series. A similar observation was made by Oberhelman. A far more significant factor in determining the viability of the bowel was, in our cases, the duration of symptoms. This is well illustrated by the fact that in most of our cases in which the symptoms had been present for 48 hours or longer, resection was necessary.

After reduction of the intussuscepted bowel, determination of its viability is essential. In the great majority of cases, the bowel immediately assumes a normal color and it is obviously safe to return it to the peritoneal cavity. In these instances, the operative procedure terminates at this point, or may be complemented by some procedure to stabilize the ileocecal region. Although the intussusception recurred in only 1 case in this series, it constitutes a serious complication. In several instances the appendix appeared to have been strangulated in the intussusceptum, its distal portion being hemorrhagic. In these cases the appendix was removed and its stump fixed to the lateral parietal peritoneum, a measure which unquestionably does limit the motility of the ileocecum.

Not infrequently, the bowel is of questionable viability after reduction of the intussusception. Its color is dark and cyanotic, and peristalsis is delayed or absent. In such instances, the involved intestine may be wrapped in warm stupes to encourage the return of circulation. Palpation of the pulsations of the mesenteric vessels may aid the operator in this decision. Often the abnormal color changes completely recede after 5 or 10 minutes, and the bowel may be replaced without hesitation or worry. One of the authors (R.J.C.) has observed on several occasions the persistence of a rounded area, measuring 2 or 3 centimeters, on the antimesenteric aspect of the terminal ileum, which appeared edematous and hemorrhagic (Fig. 1). In spite of the application of warm stupes the viability of this area of the

bowel, which probably represented the tip of the intussusceptum, could not be assured. In these cases, the replacement of the bowel into the peritoneal cavity was deemed unwise, and as a compromise procedure this area of the ileum was exteriorized by suturing the peritoneum to its margin. The muscle, fascia, and skin were packed away from this area in the closure, and 24 hours later the child was returned to the operating room, where, on removal of the packing, the exteriorized area of the ileum could be visualized readily (Fig. 2). In both instances, the abnormal color and edema had disappeared. The peritoneal sutures were divided and the closure of the defect in the peritoneum, fascia, and skin carried out.

In those cases in which reduction is impossible or in which gangrene is evident after reduction, resection of the involved bowel is necessary. Inasmuch as these changes usually occur in cases in which the symptoms have persisted for more than 24 hours, the victims are poor operative risks. For this reason, compromise measures have been suggested by various authors. One such procedure suggested for use in irreducible intussusception is the placing of a row of sutures about the neck of the intussusception, which halts its further progress, supplemented by a shortcircuiting procedure such as an ileocolostomy (5, 8). However, resection by some method is usually required, and the more commonly used procedures are: (1) exteriorization of the gangrenous bowel, or (2) resection, plus primary anastomosis. Although the surgical mortality in this series indicates that exteriorization is superior to direct anastomosis (Table II), it has been our observation that infants tolerate

TABLE II.—RESULTS OF SURGICAL TREATMENT

Operative procedure	Cases	Deaths	Mortality per cent
Simple reduction	26	4	15
Reduction and appendectomy	22	0	0
Reduction, fixation appendiceal stump	21	0	0
Reduction, excision Meckel's diverticulum	2	0	0
Reduction, extraperitonealization of bowel	2	0	0
Resection, primary anastomosis	3	2	66
Exteriorization	5	2	40

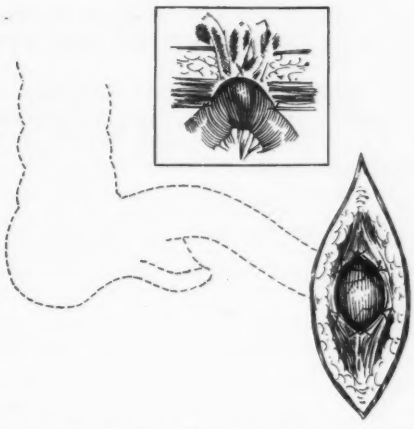

Fig. 2. Exteriorization of hemorrhagic area of ileum.

the involved ileostomy poorly. With the aid of present-day advances in anesthesia and antibiotic therapy, it is our belief that a primary anastomosis may be carried out with no greater risk than that involved in exteriorization. A rapid but accurate anastomosis can be completed if these patients are properly supported with blood and fluids during the course of the operation.

Of the 11 fatalities, 3 occurred shortly after admission and before surgical correction could be attempted. The surgical mortality in the entire series was 13 per cent, the same mortality reported in other large series (3, 6). It is noteworthy that of the 11 fatal cases, (1) in only one had symptoms existed less than 24 hours, (2) all were less than 10 months of age, (3) the majority had a substantial temperature elevation and leucocytosis, (4) peritonitis was the main cause of death in all, and (5) the intussusception was enteric in 4, representing a 44 per cent mortality in this type.

SUMMARY

In a review of 65 cases of intussusception occurring in infancy and childhood, various significant features are presented.

1. The coexistence of conspicuously enlarged ileocecal lymph nodes in 20 per cent suggests a causal relationship.

2. The importance of early diagnosis and undelayed surgical reduction of the intus-

susception is reflected in the marked increase of mortality rate with each successive 24 hour period.

3. The surgical measures employed are discussed. A conservative type of exteriorization in cases with questionable viability of the bowel is described.

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INTRAEPITHELIAL CARCINOMA OF THE CERVIX

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IN the diagnosis of uterine cancer by studies of genital smears we are constantly concerned with the identification of intraepithelial carcinoma of the cervix. We have been interested in this problem because of its importance to the patient, because of similar lesions of the cervix which occur during pregnancy, and of the possible advantages the method may have in the differential diagnosis.

Certain benign conditions engender nuclei in cervical epithelium which may be confused with the atypical nuclei of the intraepithelial lesion. However, through the co-operation of a conservative Department of Pathology we have been able to recognize cellular elements that are sometimes associated with intraepithelial carcinoma of the cervix.

We list herein certain significant data on patients who have, or have had, intraepithelial carcinoma of the cervix. We are not interested in presenting here a cytologic-pathologic discussion of the lesion. A subsequent paper based on a study of these patients, and others, will correlate pathologic diagnoses with well defined cell types found in concomitant genital smears.

METHODS AND MATERIALS

Genital smears were obtained, stained, and classified by methods described by us (1).

DATA

The patients reported were examined in the years 1947 to 1949, inclusive. Smears from 10,029 patients were studied. In 44 patients (0.44 per cent) the pathologic diagnosis was found to be intraepithelial carcinoma of the cervix.

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CLASSIFICATION OF SMEAR TYPES

No diagnosis	Insufficient epithelial elements or poor fixation
Type I	Essentially normal epithelium
Type II	Abnormal or atypical epithelium
Type III	Intraepithelial carcinoma of the cervix; questionable intraepithelial carcinoma or malignant lesion
Type IV	Cells thought to be malignant, few present
Type V	Cells thought to be malignant, many present

In Table I the clinical impressions in these 44 cases are compared with the smear interpretations.

Invasive carcinoma was not ruled out in 7 cases. The genital smears in 4 of them were interpreted as squamous cell carcinoma of the cervix. In 1 of these 4 patients the clinical impression was carcinoma. There was a clinical impression of squamous cell carcinoma of the cervix in 4 of the 44 patients. Ten patients presented no evidence of a pathologic condition. On examination 26 patients had what were thought to be benign conditions of the cervix.

Table II lists the age incidence in the 44 patients studied.

Three-fourths (75 per cent) of the lesions occurred in patients under 45 years of age. Twenty-one (47.7 per cent) of these patients were between 35 and 45 years of age.

Table III presents the smear type distribution in patients studied.

The smears in 11 cases (25 per cent) did not show elements suggestive of intraepithelial carcinoma of the cervix. Smears in 2 of these cases were unsatisfactory because of poor fixation and insufficient epithelial constituents. Twenty lesions (45 per cent) were suspected. Thirteen (29.5 per cent) were not differentiated cytologically from invasive carcinoma. Twenty-seven (61.4 per cent) of the lesions were found in 1949. Seventeen of them were detected in the last 6 months of the year.

Table IV illustrates the incidence of race and parity.

TABLE I.—CORRELATION OF CLINICAL IMPRESSION WITH SMEAR TYPE AND INTERPRETATION IN 44 CASES STUDIED

	Impression of cervix	Smear type	Smear interpretation
V.D.	Unknown	V	Squamous cell carcinoma, cervix
L.R.	Leucoplakia; cervicitis	V	Squamous cell carcinoma, cervix
R.S.	?Early carcinoma	V	Squamous cell carcinoma, cervix
M.C.	Endocervicitis	V	Squamous cell carcinoma, cervix; ?preinvasive.
A.D.	Chronic cervicitis	II	Hyperplasia of cervical epithelium
K.K.	Cervix irritated	V	Squamous cell carcinoma, cervix
V.G.	Leucoplakia, cervix	III	Suspicious of cervical carcinoma
A.H.	Chronic cervicitis	II	Few large hyperchromatic nuclei
Z.N.	Cervix normal	III	Suggestive of malignancy
A.P.	Cervical erosion	III	Many malignant appearing nuclei
M.H.	Chronic cervicitis	II	Inflammatory reaction in cervix
A.B.	Cervix normal	V	Squamous cell carcinoma, cervix
M.C.	Cervix lacerated	III	?Squamous cell carcinoma, cervix
L.H.	Chronic cervicitis	III	?Squamous cell carcinoma, cervix
G.T.	Cervix irritated	III	Atypical squamous nuclei
L.B.	Cervix normal	II	Atypical nuclei; chronic cervicitis
A.L.	Contact bleeding	III	?Squamous cell carcinoma, cervix
A.M.	Cervix lacerated; lesion	II	Chronic cervicitis
C.R.	Cervix normal	No Diag.	Poor fixation
B.B.	?Early carcinoma, cervix	No Diag.	Poor fixation
S.C.	Chronic cervicitis	III	?Intraepithelial carcinoma, cervix
E.S.	Cervix normal	V	Adenocarcinoma, cervix
A.A.	Cervix normal	III	?Squamous cell carcinoma, cervix
L.S.	Cervix irritated	III	?Squamous cell carcinoma, cervix
L.L.	Cervix normal	II	Many atypical nuclei
M.H.	Unknown	II	
D.S.	Chronic cervicitis	III	Suggestive of malignancy
B.N.	Carcinoma, cervix	V	Squamous cell carcinoma, cervix
H.S.	Cervix normal	II	Large hyperchromatic nuclei
R.H.	Cervix normal	V	Squamous cell carcinoma, cervix
M.W.	Carcinoma, cervix	III	?Malignancy
C.M.	Chronic cervicitis	III	?Squamous cell carcinoma, cervix
D.C.	Contact bleeding; lesion	III	Intraepithelial carcinoma, cervix; may be invasive
B.H.	Chronic cervicitis	III	?Intraepithelial carcinoma, cervix
H.R.	Cervical lesion	V	Squamous cell carcinoma, cervix
N.S.	Cervix irritated	V	Squamous cell carcinoma, cervix
O.M.	Cervix normal	III	?Intraepithelial carcinoma, cervix
M.P.	Chronic cervicitis	III	?Squamous cell carcinoma, cervix
C.F.	Cervix irritated	V	Squamous cell carcinoma, cervix
C.E.	Cervical lesion	I	
M.T.	Cervix normal	III	Intraepithelial carcinoma, cervix
C.C.	Unknown	III	Probable intraepithelial carcinoma, cervix
M.A.	Chronic cervicitis	V	Squamous cell carcinoma, cervix
M.M.	Unknown	III	Atypical nuclei

Six patients were pregnant when the lesions were diagnosed. Their ages were: 25, 26, 32, 34, 36, and 37 years; average 31.6 years. One of these patients has had a total hysterectomy and bilateral salpingo-oophorectomy. Five patients are being followed. Two patients have been pregnant again since the lesions were first noted.

TABLE II.—AGE INCIDENCE

Age group, years	No. patients	Subtotals
20–24	1	
25–29	6	
30–34	5	12
35–39	12	
40–44	9	21
45–49	4	
50–54	2	
55–59	2	
60–64	2	
65–69	1	11
Total		44

TABLE III.—SMEAR TYPE DISTRIBUTION

Types	No. diag.	I	II	III	V	Totals
1947			1		5	6
1948			3	7	1	11
1949	2	1	4	13	7	27
Subtotals	2	1	8	20	13	
Total						44

TABLE IV.—INCIDENCE OF RACE AND PARITY

Race	No.	Parity	No.
White	38	Nulliparas	5
Negro	6	Uniparas	1
		Multiparas	11
		Grand multiparas	16
		Unknown	11

DISCUSSION

The tables presented are self-explanatory. There are but few points that need emphasis.

It is apparent from Table I that the majority of patients who have intraepithelial carcinoma of the cervix did not show clinical signs or symptoms of the lesion.

Although this series of patients is not large, we think it significant that three-fourths of the patients were under 45 years of age and that nearly half of them were from 35 to 45 years old. Previously (2), we found the incidence of cancer highest in the 45 to 49 year age group.

Table III points out that experience is required in identifying intraepithelial carcinoma of the cervix. In interpreting this lesion from smears, the cytologist inaugurates procedures which may entail serious economic or social problems for the patient. This responsibility and that of detecting the lesion in surveys make us more conscious of the fact that investigators in this field should be exceedingly well trained, and more important, that these cytologists should work in close co-operation with conservative pathologists.

Thirty-eight of the 44 patients were white. Eighteen, 17 white and 1 negro, were private patients. We cannot speculate with confidence on such a small series, but these figures may reflect results of general education regarding cancer and probably better obstetric and gynecologic care.

The pathologic diagnosis of intraepithelial carcinoma of the cervix in pregnant patients presents a problem. We have been interested in the possibility of distinguishing, in smear preparations, the lesion which may regress during the puerperium from the one which will persist as carcinoma in situ.

It has been our experience (2) that the smear technique is not of particular value in the diagnosis of far-advanced cervical carcinomas. The lesion is clinically apparent. Moreover, cellular debris and blood usually compose smears made from patients with extensive cancer of the cervix.

We are convinced that the smear method of cancer detection is most valuable in the recognition of early cancer and of intraepithelial carcinoma of the cervix, if the smears are properly paralleled with operative specimens for pathologic studies.

CONCLUSIONS

1. Patients with intraepithelial carcinoma of the cervix comprised 0.44 per cent of 10,029 patients who were checked in the Department of Obstetrics and Gynecology during the years 1947, 1948, and 1949.

2. Clinically, 4 of these patients were thought to have carcinoma of the cervix, whereas 26 patients were thought to have only benign cervical lesions. The cervices of 10 patients appeared normal.

3. Thirty-three of the 44 patients with intraepithelial carcinoma of the cervix were under 45 years of age.

4. Six patients were pregnant.

5. Thirty-eight patients (86.4 per cent) were white.

6. Genital smears are extremely useful in detecting intraepithelial carcinoma of the cervix. However, it is believed that the diagnosis of this lesion by the smear method necessitates pathologic verification.

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HYSTEROGRAPHY AND HYSTEROSALPINGOGRAPHY

An Analysis of 2,500 Cases with Special Emphasis on Technique and Safety of the Procedure

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THE uterine cavity was visualized roentgenographically in 1910 by Rindfleisch using bismuth paste as a contrast medium. Cary and Rubin (25) independently in 1914 described the use of collargol as a contrast medium to visualize the uterus by x-ray. Since that time many reports pertaining to hysterography and hysterosalpingography have appeared, Rubin (24-29), Jarcho (12-16), Robins (21-22), Goldberger (5), and Hyams. Despite the many reports concerning the value, simplicity, and safety of hysterography and uterosalpingography during the last 40 years, (this method is still struggling for proper recognition). We believe its use has been limited because of *supposed* complications and for this reason we reviewed 2,500 cases to evaluate the safety of the method.

Fourteen hundred hysterograms were performed in the hospital by various members of the gynecological staff who employed a similar technique. Eleven hundred hysterograms were collected from the private practices of the authors. Most of the hysterograms in this group of cases were done by one of the authors (R.H.M.). Every patient was observed for at least 1 hour after the hysterogram and the following day the patient was interviewed as to pain, temperature, or bleeding. One week later a pelvic examination was done by the referring gynecologist. All immediate and delayed reactions were recorded.

The indications for uterosalpingography in our series were: (1) menometrorrhagia, (2) dysmenorrhea, (3) sterility, (4) fibroid uterus, and (5) postmenopausal bleeding. These indications will be discussed fully in a later publication.

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Contraindications were pelvic inflammatory disease, intrauterine pregnancy and purulent vaginal discharge, and serious constitutional disease. Cases of pelvic inflammatory disease were excluded from this examination only in the presence of an increased sedimentation rate, increased white blood count, or fever.

The following contrast media were employed: (1) lipiodol, (2) diodrast, (3) skiodan acacia, (4) hippuran, (5) visco-rayopaque, and (6) iodochloral.

Lipiodol was the first popular drug used for uterosalpingography and by 1922 it had superseded the other radiopaque media (i.e. sodium bromide, thorium citrate, and bismuth paste) to outline the uterine cavity. These latter media were unsatisfactory because of the severe and inadequate radiographic contrast. Sicard and Forestier (30) in 1921, employed lipiodol for the localization of tumors of the spinal cord. Its use was then extended to other cavities including the genitourinary tract. Lipiodol became associated with uterosalpingography and for many years was the sole drug employed. As the use of this iodized oil increased, some reports of undesirable reactions appeared. These included (1) emboli, (2) foreign body reaction within the tubes and peritoneal cavity, and (3) pelvic abscess. These complications will be briefly discussed.

Although there have been several cases of lipiodol entering the uterine veins (1, 3, 19, 33) pulmonary embolization following the use of this substance is uncommon (4, 8, 23). Most authors agree with E. R. Williams that this complication is usually the result of (1) direct trauma to the endometrium, (2) injection under high pressure or (3) injection when the endometrium is physiologically "deficient," i.e., during or after cessation of menstruation, or (4) when endometrium or cervix have had

recent surgical trauma, i.e., after dilatation and curettage. When these conditions are avoided, intravasation with possible subsequent embolization is uncommon. In rare instances, although extreme caution is employed, because of an anatomical variant within the uterus, this complication may occur. Such an incident was reported by Gajzago in which embolization followed the injection of lipiodol into a dilated vein of a submucous fibroid.

In many of the cases reported in the literature there was insufficient evidence to justify the diagnosis of pulmonary embolus, and often large amounts of dye were injected under great pressure. In our series when lipiodol was employed, there were no cases of intravasation of the dye into the veins or any pulmonary complications. When using lipiodol the pressure was always below 200 millimeters of mercury and the largest amount of dye used was 8 cubic centimeters. A large sinus opening into a uterine vessel is probably the most likely cause of lipiodol intravasation where proper technique is employed.

A further objection to the use of lipiodol has been the occasional fat granuloma which may form in the tubes and peritoneal cavity. A case illustrating this complication was reported by Rubin (27) in which a radiopaque pelvic mass noted on x-ray examination was removed. In our series fat granuloma within the tube occurred once when lipiodol was used. This took place in a patient who was suffering from sterility and whose tubes had been closed for many years. The uterosalpingogram was done to determine the point of closure. Operation performed 8 months later revealed a fat granuloma in the distal portion of the left tube. Therefore, we believe that granulomas occur rarely in normal tubes probably because of active peristalsis. Follow-up films would seem to substantiate this belief as this radiopaque medium has not been found in normal tubes after 24 hours.

Pelvic infection may occur following the use of any of the radiopaque media and will be discussed later in this paper.

Robins (21, 22), who has used lipiodol extensively, states that it is stable, nonirritating, nontoxic, and well tolerated by the peritoneum. He believes that it is the medium of choice. Rubin (26), on the other hand states that until a radiopaque substance will be found having the proper viscosity and density to demonstrate permeable tubal strictures and possessing that degree of resorption which leaves no residue within the tubal lumen after a few hours, thus preventing foreign body reaction, one would do well in instances of sterility to stop using iodized oil. The prevalence of this concept among those interested in sterility stimulated the investigation of other contrast media.

Titus and associates experimented with skiodan (mono-iodomethane sulfanate of sodium) which is used in intravenous pyelography. Since the viscosity of skiodan alone was too low for adequate visualization and proper handling, he added various viscous substances. Dextrose, starch, glycerine, propylene glycol, tragacanth and acacia were investigated, and the optimum solution was considered to be 40 per cent skiodan in 20 per cent acacia. This substance in the uteri of rabbits was nonirritating and histological study revealed no changes. It was used subsequently in humans by Titus and found highly satisfactory. We have used this substance as well as rayopaque extensively.

Visco-rayopaque as a medium for hysterosalpingography was introduced in 1941 by Rubin (26, 29). It has since been replaced by an almost similar drug, rayopaque (50 per cent diethanolamine salt of dioxo-3-iodo-6 methyl tetrahydropyridine-n-acetic acid). The iodine content is approximately 15 per cent. Both skiodan acacia and rayopaque have the advantage of quick absorbability and excretion which obviate the danger of embolization and foreign body reaction. Their quick absorbability can, however, be disadvantageous in sterility investigations for it precludes the possibility of a late film which in some cases demonstrates tubal permeability.

TECHNIQUE

It is generally recognized that the optimum time for the performance of the procedure is one week after the cessation of the menstrual flow. The patient is placed on a radiographic table equipped with Bucky dia-

phragms. Stirrups may or may not be used. Bimanual examination is performed to determine the position, size, mobility of the uterus, and to note the presence of any palpable pelvic pathologic condition. A preliminary film of the abdomen is taken. The patient is placed in the lithotomy position. A fiber, bivalved speculum is introduced into the vagina and the cervix is exposed and painted with antiseptic solution. The anterior lip of the cervix is then grasped with a tenaculum and the uterine sound is introduced into the uterine cavity to note the direction and depth of this structure. This is of great importance as the cannula must be introduced in a similar direction. The iodized material is then introduced through the cannula which may have an attached manometer. The material is injected slowly and gently. The technique with hysterosalpingography and hysterography differs. In hysterography 1 cubic centimeter of dye is injected and a film is taken. Fractional amounts of opaque material up to 3 or 4 cubic centimeters of dye are introduced and films are taken at each injection. The fractional method was described by M. N. Hyams in 1935. The radiopaque medium is injected under low pressure, and if any obstruction is encountered, the injection is discontinued. A film in the oblique position is valuable as it facilitates the interpretation of filling defects in the uterine cavity, and demonstrates lesions on the posterior uterine wall.

The procedure differs in sterility cases in two respects. First, the amount employed must be larger. The uterine cavity and tubes can be visualized in 95 per cent of cases with 6 cubic centimeters of radiopaque medium and minimal pressure. Larger amounts of dye are necessary in the occasional case of an enlarged uterine cavity or in the presence of a large hydrosalpinx (Figs. 1 and 2). If fluoroscopic control is used the course of the dye through the uterus and tubes may be visualized and the exact amount necessary for visualization injected.

The technique in uterosalpingography again differs, depending upon whether water soluble or oily media are employed. The injection with lipiodol is discontinued when an obstruction to the flow of dye at 200 millimeters of mercury pressure is encountered. It is important to observe this rule with lipiodol as intravascular penetration may result in an embolus. If the films do not reveal the opaque material in the peritoneal cavity (Fig. 3), a 24 hour film (Fig. 4) may be taken which helps in the differentiation of organic and functional tubal obstruction. When the water soluble media are employed, the dye should reach the peritoneal cavity, since a delayed film cannot be taken because of rapid absorbability.

The finding of closed, but otherwise normal tubes, by means of these media, does not necessarily indicate organic pathology as the closure may be due to spasm. Since intravascular penetration followed by embolization cannot occur with water soluble media, we have employed pressures up to 250 millimeters of mercury when necessary. In most cases when the tubal closure is due to spasm this high pressure is sufficient for the radiopaque medium to reach the peritoneal cavity. There is an occasional case, however, in which the tubes are so spastic as to withstand this pressure. It is in these cases that lipiodol is helpful, as a 24 hour film may differentiate between spasm and organic closure (Figs. 3 and 4). It should be noted that when the closure is at the cornual junction, lipiodol also is of no value as the dye must reach the tubes for a 24 hour film to be useful. It is not always essential for the dye to reach the peritoneal cavity as roentgenographic study (Fig. 5) of the tubes may indicate whether or not they are normal.

By employing a simple method, the operator can sometimes determine during the course of the injection when the dye has entered the tubes. Following the initial injection of 2 cubic centimeters the dye can be withdrawn. If the entire amount is recovered one may be reasonably certain that the dye has not entered the tubes. When the entire amount cannot be withdrawn, it indicates that the dye has passed the uterotubal junction and entered the tubes.

Complications have been divided into those due to the dye and those due to the procedure.

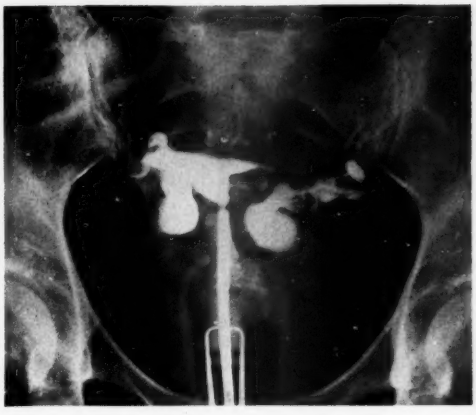

Fig. 1. The uterine cavity is normal in size, shape, and position. The distal ends of both tubes are closed. There is a bilateral hydrosalpinx. Nine cubic centimeters of water soluble radio-opaque media used.

Fig. 2. Both tubes are closed at its distal ends. There is present a large bilateral hydrosalpinx. Twelve cubic centimeters of water soluble radio-opaque media were easily injected.

COMPLICATIONS DUE TO CONTRAST MEDIA

Complications due to the contrast media are: (1) pain, (2) peritonitis, (3) endometritis, (4) allergic phenomena, and (5) emboli.

Pain. Eighty per cent of the patients experienced some degree of pain varying from a few moments to several hours when the dye entered the peritoneal cavity. This pain varied with the amount of contrast media injected and the different contrast media employed. It should be emphasized that pain did not occur when the radiopaque substance did not enter the peritoneal cavity or tubes. The pain was most severe with visco-rayopaque and of less intensity with the other substances. Visco-rayopaque was so irritating that it became necessary for us to discard its use in uterosalpingography. Recently this substance has been altered and we have since used it in a large group of cases with much better results. The new product is known as rayopaque. Lipiodol caused the least pain. The pain was slightly more exaggerated with skiodan acacia and rayopaque. The contact of the contrast medium with the peritoneum was usually the most important factor in producing pain. Some patients have the sensation of a desire to defecate indicating that the contrast medium has probably reached the cul-de-sac. A few patients vomited following the procedure. Recently, we have administered 50 milligrams of demerol prior to uterosalpingography, and the pain has been considerably diminished.

Peritoneal irritation. Those patients who had severe prolonged pain exhibited some signs of peritoneal irritation such as lower abdominal rigidity, tenderness, vomiting, and occasional fever. There were 14 patients in a series of 1,014 where the dye reached the peritoneal cavity, who developed these symptoms. This reaction occurred regardless of the contrast media used in our series. A description of one of these cases follows:

P. S., a 30 year old female suffered from involuntary sterility of 3 years' duration. Tubal insufflation on repeated occasions revealed closed tubes. Uterosalpingogram was taken and revealed both tubes to be patent. Pressure of 200 millimeters of mercury was necessary for the dye to pass through the tubes into the peritoneal cavity. A total of 8 cubic centimeters of skiodan acacia was used. Immediately following the uterosalpingogram the patient complained of severe pain in her lower abdomen and she vomited. The pain lasted for several hours during which time her lower abdomen was moderately rigid and tender. The symptoms subsided and pelvic examination was negative. A sedimentation rate and white blood count were normal. There was never any history of previous pelvic inflammation. We, therefore, assumed that the dye irritated the peritoneum sufficiently in this case to produce a mild chemical peritonitis. The other 13 cases which we

Fig. 3. The uterine cavity is normal in size, shape, and position. Both tubes are partially visualized. No dye is noted in the peritoneal cavity. It is impossible to state from this film whether or not the tubes are patent. (See Fig. 4.) (Iodized oil was used.)

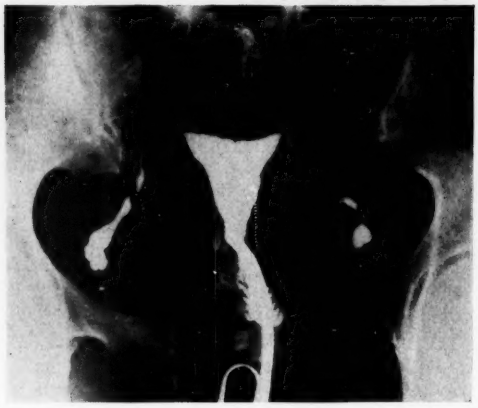

Fig. 5. The cervical canal is dilated and serrated (chronic endocervicitis). The uterine cavity is slightly enlarged. The distal third of both tubes is slightly dilated. This type of tube is usually associated with nonpatency. Compare with Figure 14 illustrating a normal right tube.

observed were essentially similar to the one just described.

Endometritis. A total of 450 uteri and tubes were excised and studied at intervals of 1 day to 1 week following uterosalpingography. No reaction was noted in the cases in which skiodan acacia, rayopaque, hippuran, and diodrast were used. In 8 cases following the use of the old visco-rayopaque the following reaction was noted. The endometrium was swollen, hyperemic, edematous, and there was an infiltration of polymorphonuclear leucocytes.

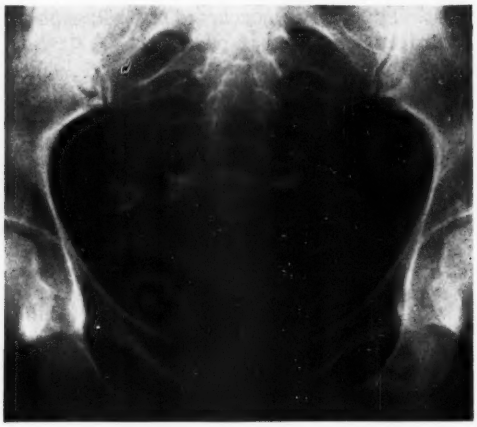

Fig. 4. Twenty-four hour film showing radio-opaque material within the peritoneal cavity proving tubal patency. Iodized oil used.

Allergic phenomena. Nine patients developed urticaria following the use of the water soluble media. In 8 of these cases the radiopaque medium was noted in the uterine circulation.

Emboli. In our series of 300 cases in which lipiodol was used, emboli did not occur. Intravasation, however, did occur in 38 cases in which soluble media were employed (Figs. 6, 7, 8). This was due probably to two factors: first, the low viscosity of the media and, second, the occasional use of pressure above 200 millimeters of mercury. Since there is no danger of an embolus with these media, pressure of this magnitude was sometimes used to overcome tubal spasm.

COMPLICATIONS DUE TO THE PROCEDURE

The following complications occur rarely: (1) hemorrhage, (2) acute exacerbation of chronic pelvic inflammatory disease, (3) perforation of the uterus, (4) shock, (5) visualization of the uterine vascular structure, (6) introduction of radiopaque medium into a pregnant uterus.

Hemorrhage. Staining following uterosalpingography is common. However, hemor-

Fig. 6. The uterine cavity is not visualized. The uterine and several pelvic vessels are partially visualized. A repeat hysterogram at a later date revealed similar findings. No excess pressure was used.

Fig. 7. The uterine cavity is slightly enlarged. Both tubes are closed. The uterine sinuses on the left side are visualized. A pressure of 250 millimeters of mercury was used in this case.

rhage is rare. Three patients experienced considerable bleeding unrelated to their periods following uterosalpingography or hysterography. In 2 cases bleeding ceased in 3 days. In these cases a hysterogram was performed because of bleeding, and in 1 case a submucous fibroid (Fig. 9) was found and in the other an endometrial polyp (Fig. 10). The third case of hemorrhage is reported in more detail as it indicated a very unusual complication.

I.R., a 40 year old married female had menorrhagia and metrorrhagia for 3 months. Her past history was essentially negative. Her periods were always regular, prior to her present illness occurring every 30 days and lasting 4 days. Her present illness started 3 months ago with bleeding which has been unusually severe during the past 2 weeks with the passage of clots. Pelvic examination revealed an irregular nodular thickening extending into both adnexal regions. The cervix could never be adequately visualized. A hysterogram was performed to exclude the presence of a submucous fibroid. A speculum was inserted and although the cervix was not definitely seen, an opening was noted through which a sound could be passed. Very little resistance was encountered and it was felt that the sound had entered the uterine cavity or possibly the peritoneal cavity. The dye was injected and immediately following this procedure, the patient bled considerably. Films (Fig. 11) revealed no visualization of the uterine cavity but radiopaque material was present in the peritoneal cavity. Within 24 hours the hemoglobin had fallen to 50 per cent and exploratory operation was done. The uterine cavity was found to be slightly enlarged and adherent to the cul-de-sac. Several bluish puckered nodules, some single and some multiple, were involving both uterosacral ligaments and the pelvic floor. Both ovaries were cystic and hemorrhagic. An opening was seen in the pelvic floor, on the left side, in the region through which a probe could be passed into the vagina. The tissues in this area were friable and bled easily. A panhysterectomy was performed. The pathological report was endometriosis involving both tubes, ovaries, and the pelvic floor. The hysterogram was bizarre in this case and we were reasonably sure that the dye had entered the peritoneal cavity.

Fig. 8. The uterine cavity is normal in size, shape, and position. No filling defects are noted. The uterine and several pelvic vessels are visualized. No pressure was used in this case.

Fig. 9. The uterine cavity is enlarged and globular in outline. Within the uterine cavity there is a filling defect due to a submucous fibroid. A small calcified fibroid is seen to the right of the uterine cavity.

Fig. 11. The uterine cavity is not visualized. Dye is irregularly distributed in the peritoneal cavity and cul-de-sac.

This case demonstrated the necessity for strict adherence to proper technique as the procedure should not have been performed unless the cervix could be adequately visualized.

Acute exacerbation of chronic pelvic inflammatory disease. Seven times in our series, patients developed pelvic peritonitis. In all of these cases there was a history of previous pelvic inflammatory disease, and the uterosalpingogram was made to demonstrate tubal patency. In 4 of these 7 cases, pressures higher than 250 millimeters of mercury were used in order to visualize the tubes, for repeated Rubin tests had demonstrated nonpatency. Despite these high pressures the tubes were not visualized and in 2 of these cases the uterine vessels were visualized.

In one of the 7 cases no excess pressure was used and a large hydrosalpinx was noted. Four of the patients recovered on bed rest and treatment with antibiotics and chemotherapeutic agents. Three required colpotomy for drainage of pelvic abscesses. The following cases are illustrative.

Fig. 10. The uterine cavity is small. There is a small circular filling defect due to an endometrial polyp.

CASE 1. The patient was a 34 year old female who was a sterility problem. Four years previous, she had a pelvic infection following a dilatation and curettage. At that time she was bedridden for 4 weeks with severe lower abdominal pain and a profuse purulent vaginal discharge. She had no subsequent recurrences. Following the injection of skiodan and acacia, under pressure of 250 millimeters of mercury, the patient complained of severe left lower quadrant pain. A few hours later, her lower abdomen was moderately rigid and she had a temperature of 100 degrees. The patient was treated with bed rest, penicillin, and sulfadiazine. Pelvic examination 1 week after the test, revealed bilateral pelvic masses. The symptoms and signs gradually disappeared.

CASE 2. A 24 year old female, 2 years ago developed pelvic inflammatory disease. She was a nulligravida, who was referred because of lower abdominal pain and metrorrhagia. A hysterogram was performed in order to study the uterus and tubes. No excess of pressure was used. The films revealed a large, left hydrosalpinx (Fig. 12). The patient devel-

Fig. 12. The uterine cavity is normal in size, shape, and position. The right tube is closed in its proximal third. The left tube reveals a fairly large hydrosalpinx. No dye is noted in the peritoneal.

Fig. 13. The uterine cavity appears to be slightly enlarged. Within the uterine cavity there is a fairly large filling defect, which was interpreted as a submucous fibroid and later proved to be an intrauterine pregnancy.

oped a pelvic abscess which was drained through the posterior fornix. She recovered with bed rest, penicillin, and sulfadiazine.

There are several possible ways in which this complication may occur: (1) It may be an exacerbation of an old infectious process, or (2) it may be a newly formed infection, or (3) it may be an allergic reaction. Although any or all of these methods may operate singly or together it is our impression that the pelvic cellulitis is a result of trauma to a previously diseased tissue with spread of the infection via the lymphatics and blood vessels.

Perforation of the uterus. Before injecting the contrast media, a sound is passed into the uterus. This serves the dual purpose of slightly dilating the cervical os and determining the depth and direction of the uterine curve. Pelvic examinations cannot always indicate the position of the uterus, particularly in obese persons.

In 1 case in our series, the uterine sound was introduced and it entered for a distance of 4 inches without encountering any resistance. The dye was injected and a study of the films showed radiopaque substance in the peritoneal cavity and none in the uterus. The uterus had been perforated and the dye injected through the perforation. The indication for hysterography was menometrorrhagia in a 37 year old female. It is interesting to note that despite the uterine perforation, the patient had very little pain and experienced no peritoneal reaction. Because of the soft consistency of this uterus, the possibility of an incomplete abortion was considered. A pregnancy test was therefore performed and found to be negative. Dilatation and curettage were performed at a later date with the following findings. The uterine cavity was enlarged and a considerable amount of tissue obtained. The uterus was found to be soft in

Fig. 14. The right tube reveals no evidence of any abnormality and is patent. The left tube reveals a circular filling defect about 1½ centimeters in diameter. Dye can be seen in the peritoneal cavity adjacent to the uterus on the right and above the left tube. Fluoroscopically, a small portion of this dye could be seen passing through a pinpoint opening in the middle of the left tube into the peritoneal cavity. The remainder came through the fimbriated extremity of the left tube.

consistency. Microscopic report revealed hyperplastic endometrium and there was no evidence of malignancy.

This complication is most unusual and it occured only once in our series.

Shock. Mild peripheral vascular collapse was noted in 3 cases. The dye had entered the peritoneal cavity in all of these. The shock was mild and consisted of a drop in blood pressure, rapid pulse and profuse perspiration with rapid recovery. Whether this reaction was due to pain or to a similar phenomenon to that seen when the pleura is entered by a needle or following a minor surgical procedure is open to conjecture.

Dye entering the uterine vascular structure. Dye entered the uterine vascular structure 38 times in our 2,500 cases. In all of these the water soluble media were used (Figs. 6, 7, 8). In some, the tubes were opened, in others closed. In 3 cases the procedure was repeated at a later date, and in 2 the radiopaque medium again entered the uterine vessels. This indicates that in some cases, the uterine sinuses are sufficiently patent to permit the entrance of radiopaque medium with ease. In 1 case, the uterine sinuses were outlined without visualization of the uterine cavity. The procedure was repeated at a later date and the same findings noted. At operation, this uterus revealed extensive adenomyosis.

The possibility of an embolus would be entertained with lipiodol but not with the rapidly absorbed water soluble radiopaque substances.

Introduction of dye into a pregnant uterus. Two patients with unsuspected intrauterine gravidities had uterosalpingograms for sterility. Both patients had histories of menometrorrhagia. The uterosalpingogram revealed a circular filling defect, the nature of which was uncertain. In the first case a submucous fibroid (Fig. 13) was suspected, but since the patient was only 22 years of age it was decided to observe her. Since amenorrhea persisted, a pregnancy test was done and found to be positive. The patient carried to term and delivered a normal child. The second case was similar to the first and again the hysterosalpingogram did not interfere with the normal course of the pregnancy.

Radiography in ectopic pregnancy. One case is summarized.

B. S. a 22 year old female with a negative past history and a present illness of menorrhagia and metrorrhagia of 2 months' duration, had never missed a period and pelvic examination was negative. A pregnancy test was done which was negative. Dilatation and curettage had been performed 2 weeks prior to the uterosalpingogram and the report revealed a proliferative endometrium. Despite the curettage the patient continued to bleed and a uterosalpingogram was made to further elucidate the problem. This revealed the uterine cavity to be normal in size and shape. The right tube showed no abnormality and was patent, but the left tube (Fig. 14) revealed a circular filling defect about 1.5 centimeters in diameter near the center. There were no ill effects from the hysterogram. A diagnosis of left tubal pregnancy was made and the patient subjected to exploration. A tubal pregnancy was found at the site of the circular filling defect which was described above.

Although an ectopic pregnancy was suspected in this case, the laboratory findings were so completely negative that laparotomy was postponed. The hysterogram was not done to visualize the ectopic pregnancy but, as previously stated, further to elucidate the cause of the bleeding. The filling defect corresponded exactly to the site of the ovum. In order to determine whether uterosalpingography can be performed more routinely in the diagnosis of ectopic pregnancy this procedure has been performed in 15 cases of suspected unruptured ectopic pregnancy with no complications (18). The diagnosis was made and confirmed in 10. These cases further illustrate the safety of this procedure.

COMMENT

The complications due to the contrast media are not serious nor do they cause any permanent harm to the patient. When the water soluble media enters the tubes and peritoneal cavity pain occurs but this can be adequately controlled with demerol. The quickly absorbing contrast media do not cause any damage to the tissues and embolization does not occur. We never encountered permanent injury to the tubes or embolization from lipiodol; these complications, however, have been reported in the literature. The instances of allergic phenomena are few.

To summarize the relationship of the drugs to the safety of the procedure we can state that the quickly absorbing media, except for a moderate degree of pain, are harmless. Lipiodol on rare occasions may cause embolization and a granuloma within a previously diseased tube.

The complications of the procedure itself are relatively few. There were 2 cases of hemorrhage, one of short duration which required no therapeutic measures, the other was not the fault of the procedure but of technique and the condition encountered. Pelvic inflammatory disease was the most serious complication encountered. It occurred 7 times in our series of 3,500 cases. We did not observe this complication in any case where there was no history of previous pelvic inflammatory disease.

Perforation of the uterus occurred only once in our series and it was an accident.

It is difficult in so large a series of cases to avoid the introduction of dye into a pregnant uterus expecially when there is no indication that this condition exists. It is not practical to perform a pregnancy test on every case prior to uterosalpingography. All pregnancies observed in our series remained intact following hysterosalpingography.

The perfect contrast media for uterosalpingography is as yet not available; however, we have found the water soluble media very satisfactory despite the fact that it does not permit a 24 hour film and therefore patency is sometimes not established. They also have the slight disadvantage of producing some pain. The more viscous materials are excellent for hysterography but when employed to visualize the tubes they may in rare instances result in fat granulomas and emboli. Although the ideal medium for hysterography and hysterosalpingography has as yet not been found, complications from the substances available are so few that there should be no hesitation in the use of the procedure when indicated.

CONCLUSIONS

1. A review with careful follow-up is presented of 2,500 cases studied by means of hysterography and hysterosalpingography.

2. The technique, various contrast media, and the complications resulting from the procedure have been described and discussed.

3. The relatively infrequent complications and the safety of the procedure is noted.

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INTERNAL DERANGEMENT OF THE TALOFIBULAR COMPONENT OF THE ANKLE

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PERSISTENT or intermittently recurring pain and swelling over the fibular aspect of the ankle are not infrequent sequelae of an inversion sprain, producing a disturbance to which the patient may refer as a "weak" or "trick" ankle. Routine roentgenograms may be negative or they may reveal some ossification in the region of the fibular collateral ligament (6, 12). Various authors have pointed out that such symptoms can result from a rupture of the lateral ligament (4, 7, 9) causing instability of the talus within the ankle mortise, with roentgenograms of the fully inverted ankle demonstrating a tilting of the talus. Other relatively uncommon causes of recurrent catching or "giving-way" of the ankle are osteochondritis dissecans of the talus (5) and osteochondromatous loose bodies (11).

In our experience, however, the majority of cases in which pain and swelling follow injury to the lateral ligament fail to show ligamentous instability on clinical and radiological examination. Furthermore, if the symptoms are carefully analyzed, the most logical explanation for their cause would appear to be the pinching of some tissue mass within the talofibular articulation. If this is correct, it should be logical to expect that cure can be affected by removal of this deranging factor. We have therefore resorted to surgical exploration in those patients with symptoms persisting despite such conservative measures as immobilization, adhesive strapping, elastic support, shoe correction and physical therapy. Although our series of cases is still very small, we have consistently encountered in examination of patients a mass of hyalinized connective tissue arising from the anteroinferior portion of the talofibular joint capsule and extending into the joint. Removal of this mass of tissue has relieved the symptoms.

CASE REPORTS

CASE 1. J. C., aged 22 years, a professional football player, sustained an inversion sprain of the left ankle during a game in September, 1948. He had adhesive strapping for about 2 weeks, followed by physical therapy, but he continued to complain of pain over the fibular aspect of the ankle. When he attempted to turn sharply while running, he experienced a painful snapping sensation anterior to the fibular malleolus and he described radiation of the pain upward to the head of the fibula. He recalled that in 1946 he had incurred a severe sprain of the left ankle during a college football game and had been disabled for about 4 weeks, but he had made an apparently complete recovery.

At the initial examination on October 8, 1948, he presented a click on motion of the left ankle and a tender thickening just anterior to the fibular malleolus. Compression of the fibula against the talus produced a sharp pain in the lateral aspect of the ankle. Roentgenograms (Fig. 1) revealed a spur arising from the anterior lip of tibia but no bony pathology in the talofibular region. There was no tilting of the talus on inversion of the ankle.

At operation on October 20, 1948 the lateral compartment of the ankle was exposed through a vertical incision placed anterior to the fibular malleolus. A dense mass of firm white tissue of fibrocartilagenous consistency, about 5 millimeters in diameter, was found arising from the joint capsule immediately in front of the tip of the fibula and extending into the ankle joint where it was firmly wedged between the talus and the fibula. Because this mass looked so much like a knee meniscus, we decided on the term "meniscoid" to describe it. There was no instability of the talus, but inversion and eversion of the ankle demonstrated clearly the pinching of the meniscoid mass between the fibula and the talus. Figure 14b is a sketch of the condition.

The meniscoid mass was removed. Only after this was performed was it possible to pass a fine probe between the fibula and talus down to the posterior aspect of the joint. Five days postoperatively a walking cast was applied. This was worn for a week and was followed by elastoplast strapping. Cautious running was resumed 2 weeks postoperatively on November 3, 1948. One week later he returned to athletics. He has remained symptom-free.

Report of the microscopic examination of the tissue removed from the ankle (Fig. 2) was "dense connective tissue suggesting ligament and fibrocartilage."

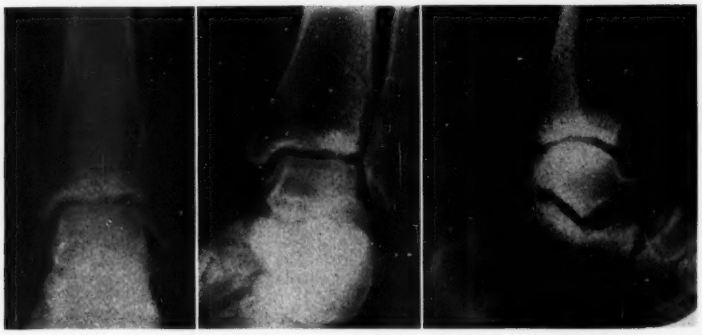


Fig. 1. Case 1, J. C. Roentgenograms of ankle, including anteroposterior view with strong inversion. No bony pathological process is present in the fibular compartment. There is no instability of the talus.

CASE 2. V. S., aged 23 years, a professional football player sprained the lateral ligament of his left ankle early in September, 1948. He made an apparently prompt recovery with adhesive taping, but on October 5, 1948, the left ankle became sprained again. Taping was reapplied. On October 12, 1948, with the joint still strapped, the ankle "locked" and he was unable to move it for a few minutes, during which there was severe pain over the lateral aspect of the joint. He gradually worked the ankle free by cautious manipulation.

Examination on October 22, 1948, 6 weeks after the initial sprain, revealed mild thickening and localized tenderness just anterior to the fibular malleolus. Roentgenograms revealed no bony pathology (Fig. 3).

At operation on October 27, 1948 a fibrocartilagenous "meniscoid" band, almost identical with the one described in Case 1, was found in the talofibular compartment and was removed. There was no instability of the talus.

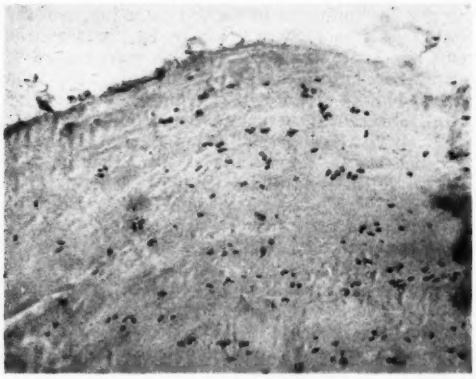


Fig. 2. Case 1. J. C. Photomicrograph of tissue within the ankle, as sketched in Figure 14b, revealing "dense fibrous connective tissue resembling ligament and fibrocartilage."

The microscopic section of the tissue (Fig. 4) was also much the same as in Case 1. The same postoperative care was followed. The patient returned to athletics 3 weeks postoperatively. He has had no further symptoms.

CASE 3. A. M., aged 26 years, a professional football player, sustained an inversion sprain of the left ankle in November, 1948. He continued to have recurrent pain over the outer aspect of the ankle whenever he attempted to run and he added that the pain radiated to the head of the fibula. Examination on April 30, 1949, revealed mild localized swelling over the fibular aspect of the left ankle. Roentgenograms showed no bony pathology.

At operation on May 28, 1949, a mass of fibrocartilagenous consistency was found impinged between the talus and fibula. Just above this there was a free cartilagenous loose body, oval in shape, about 3 millimeters in diameter. No instability of the talus could be demonstrated.

The tissue lying within the lateral compartment of the ankle was removed (Fig. 6). The postoperative walking cast was discarded 2 weeks later. Full athletics were resumed 3 weeks after operation. The disability has not recurred.

In each of these 3 cases the disturbance within the lateral component of the ankle mortise was a derangement due to repeated pinching of an adventitious tissue mass between the lateral border of the talus and the articular surface of the fibula.

CASE 4. C. M., a 13 year old boy, sustained an inversion twist of his right ankle on June 8, 1934. In addition to clinical evidence of a typical inversion sprain involving the fibular collateral ligament he had radiological evidence of a tiny chip fracture of the os calcis at its anterior margin. A walking cast was worn from June 6 to June 19, 1934.

Fig. 3. Case 2. V. S. Roentgenograms of ankle, including inversion view, showing no bony pathological process or ligamentous instability.

The patient returned 2 years later on June 23, 1936. He stated that 10 days previously, after running track, he had experienced pain and swelling over the outer aspect of the right ankle but that he had improved spontaneously. There were no findings on clinical examination.

Six months later, on January 30, 1937, the boy again presented himself, complaining of pain in the right ankle on exertion and intermittent swelling. Examination revealed a definite click over the fibular aspect of the joint on inversion. Roentgenograms (Fig. 5) revealed a free ossicle anterior to the tip of the fibular malleolus. Operation was advised in the belief that the loose bony fragment was responsible for the symptoms.

Surgery was performed on March 17, 1937. A bony fragment 1 centimeter in diameter was encountered at the interior inferior margin of the fibular malleolus. Arising from this chip, a "meniscoid" band of firm white tissue extended into the lateral portion of the ankle mortise. The meniscoid band and the bony fragment were removed. A definite indentation was then demonstrable on the lateral wall of the talus.

Full weight bearing was allowed 10 days later. At the time the patient was observed last on December 29, 1939, he had no symptoms in the right ankle.

CASE 5. R. L., a 34 year old male, was first seen in May 1948. He complained of a "weak" right ankle with recurrent turning over in varus, pain and swelling over the lateral aspect of the joint, and a feeling of insecurity on walking. These symptoms began after an inversion sprain of the ankle incurred about 12 years previously.

Examination revealed a little irregularity of the distal end of the right fibula. Compression of the fibula against the talus produced pain over the lateral aspect of the joint. Roentgenograms (Fig. 7) revealed a free ossicle just anterior to the tip of the lateral malleolus.

At operation performed May 28, 1948 a 1 centimeter ossicle was found just under the anterior talofibular ligament (Fig. 8). Arising from the deep surface of this bony fragment a firm meniscoid band extended into the space between the fibula and talus (Fig. 9). The ossicle and band were removed.

The microscopic section (Fig. 10) of the soft tissue specimen was reported as revealing "hyalinized connective tissue lined by synovia."

The patient had no further ankle symptoms.

Cases 4 and 5 illustrate derangements of the talofibular articulation associated with an island of ectopic ossification within or just under the anterior talofibular ligament or anterior fasciculus of the fibular collateral ligament. Nevertheless the clinical symptoms were apparently due chiefly, as in the first 3 cases, to the soft tissue mass within the joint. The bony ossicle probably is similar to the ossification at the medial ligament of the knee which may be seen after the knee-joint injury, and which is sometimes but not always associated with injury of the medial meniscus.

Fig. 4. Case 2. Photomicrograph of tissue removed from ankle mortise, practically identical with Figure 2.

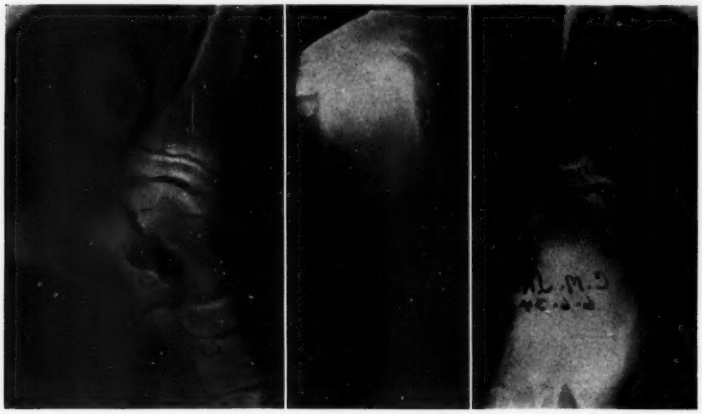


Fig. 5. Case 4. C. M. Roentgenograms revealing ossicle in anterior talofibular ligament. Note that the ossicle, lying *anterior* to the fibula, is not visualized on the routine anteroposterior view of the ankle.

CASE 6. A. B., a 19 year old male, was seen on October 20, 1939. He complained of chronic pain over the outer aspect of the right ankle with recurrent "giving way" and snapping of the joint. He stated that these symptoms followed a severe sprain of the ankle incurred 4 years previously. He added that 1 year prior to his first visit he had "fractured" the right ankle playing football and was treated in a cast. After the treatment for the fracture he continued to have pain over the lateral aspect of the ankle, radiating at times upward toward the knee.

Examination revealed generalized swelling about the right ankle, especially over its lateral aspect. Inversion revealed a click and pain over the talofibular articulation. Tenderness was elicited anterior to the fibular malleolus and at the tip of the tibial malleolus.

Roentgenograms revealed a loose chip or ossicle at the tip of the medial malleolus.

A clinical diagnosis was made of chronic traumatic arthritis.

Operation was performed on October 24, 1939. The loose chip was removed from the tibial collateral ligament just below the malleolus; there was no connection between the chip and any intra-articular structure. A second incision was made exposing the talofibular articulation, where a pad of thickened synovial membrane was encountered and removed.

The microscopic examination of the soft tissue specimen (Fig. 11) revealed "marked chronic synovitis with evidence of old hemorrhage."

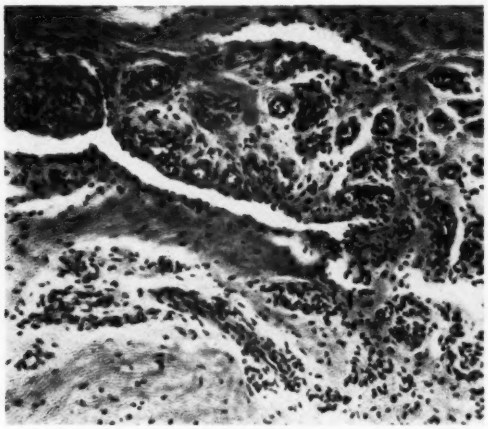
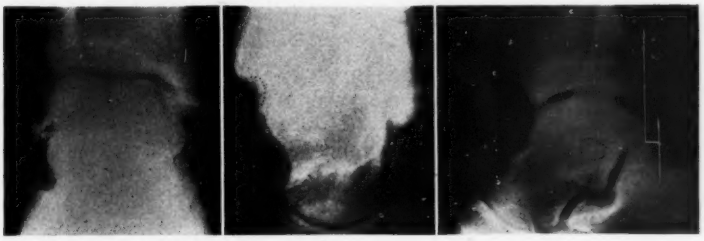


Fig. 6. Case 3. A. M. Photomicrograph of tissue removed from left ankle, showing hyalinized connective tissue and chronic synovitis.

In this case, although the para-articular ossification involved the tibial collateral ligament, the clinical symptoms were referred chiefly to the fibular compartment of the joint, where the major pathology was encountered. We have here a demonstration not only of the importance of careful clinical localization of the symptoms and findings but also of the relative innocuousness of the ectopic island of ossification when it does not impinge within the joint.

CASE 7. I. S., a 33 year old housewife, was first seen on November 12, 1949, complaining of pain and swelling over the lateral aspect of the right ankle. She stated that she had sprained the ankle 9 weeks previously when she fell and that the pain was be-



a b c

Fig. 7. Case 5. R. L. Roentgenograms of ankle showing ossicle in area of anterior talofibular ligament. a, Routine anteroposterior view. b, Anteroposterior view through tarsal region. c, Lateral view.

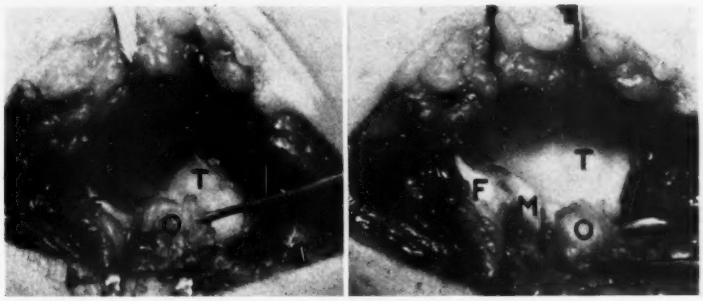


Fig. 8. left, Case 5. R. L. Photograph of operative findings. The lower retractor is on the lateral aspect of the incised anterior talofibular ligament. *F*, Fibula; *T*, talus; *O*, ossicle arising from anterior talofibular ligament.

Fig. 9. Case 5. R. L. Photograph of operative finding. Ossicle, *O*, has been dissected from tip of fibula and anterior talofibular ligament and then retracted with towel clip, thus revealing meniscoid, *M*, lying between fibula and talus.

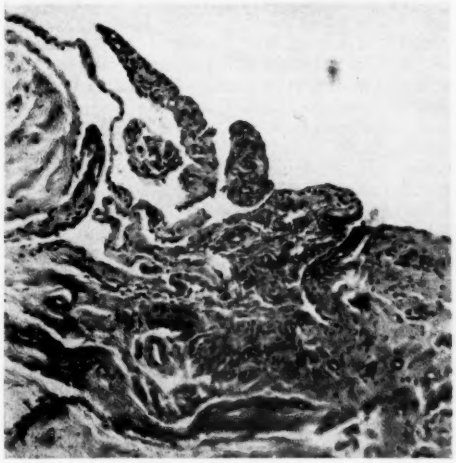


Fig. 10. Case 5. R. L. Photomicrograph showing hyalinized connective tissue covered by synovial lining.

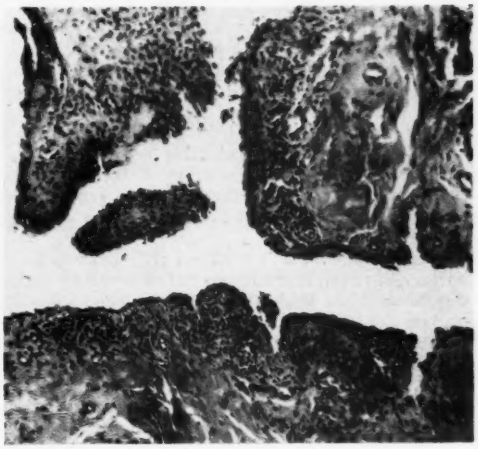


Fig. 11. Case 6. A. B. Photomicrograph showing marked chronic synovitis and old hemorrhage.

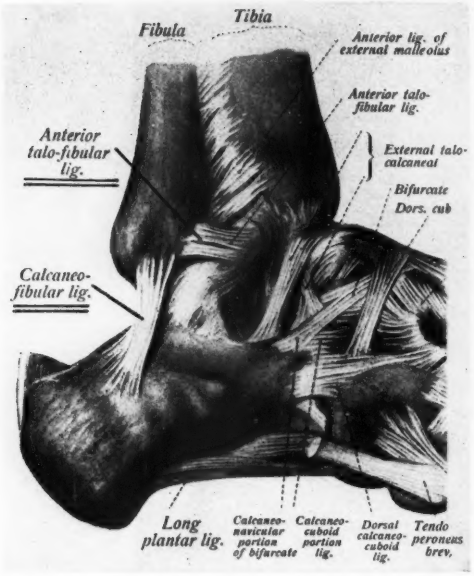


Fig. 12. From Sabotta's *Atlas and Textbook of Human Anatomy*. The ligaments of the ankle seen from above and from the outer side. (Reprinted by permission of Stechert-Hafner, Inc., New York.)

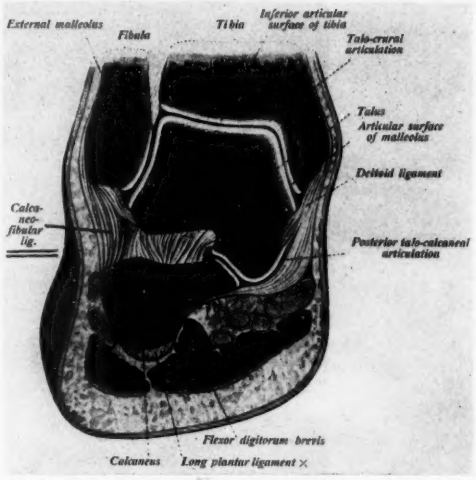


Fig. 13. From Sabotta's *Atlas and Textbook of Human Anatomy*. Frontal section through the ankle and posterior talocalcaneal joints. (Reprinted by permission of Stechert-Hafner, Inc., New York.)

coming progressively worse, with recurrent giving way and sharp pain over the lateral aspect of the joint traveling upward to the outer side of the knee. She gave a history of a very severe sprain of the right ankle incurred in 1928.

Examination revealed a tender thickening over the right talofibular articulation and inversion produced a painful click in this region. Compression of the fibula against the talus was extremely painful. Roentgenograms revealed no bony pathological state.

At operation performed on December 2, 1949 a mass of white fibrous connective tissue was found attached to the articular surface of the fibula and the articular cartilage of the fibula was rough. The fibrous tissue was removed and the rough cartilage was shaved smooth.

CASE 8. R.C., an 11 year old girl, was examined on July 8, 1949. She complained of frequent giving way of the right ankle with pain over the fibular aspect of the joint and she stated that her symptoms began after a fracture of the right ankle incurred about 3 years previously.

Examination revealed a tender thickening anterior to the right fibular malleolus. Roentgenograms revealed no bony pathological process.

Strapping with elastoplast gave temporary relief. The elastoplast was removed on July 22, 1949, and a leather anklet was applied. The symptoms persisted. An outflared right heel with an outer wedge, prescribed on September 19, 1949, did not result in improvement.

Operation was performed on December 27, 1949. A large "meniscoid" mass was found between the talus and the tip of the fibula, arising from the capsule directly anterior to the fibula. The mass was removed. The synovial lining was thickened and hyperemic. There was no instability of the talus.

CASE 9. C. M., a 17 year old girl, sprained her right ankle while running about July 29, 1949, and adhesive strapping was employed for 3 weeks. She returned on October 25, 1949 complaining of chronic pain and weakness in the right ankle, and examination revealed localized thickening and tenderness over the fibular aspect of the ankle. There was no radiologically demonstrable pathology. An elastic anklet was prescribed but the symptoms remained unchanged.

Operation was performed on December 27, 1949. A band of firm hyalinized tissue was found arising from the joint capsule directly anterior and distal to the tip of the fibula, extending into the interval between the talus and fibula. This tissue was removed.

In Cases 7, 8, and 9, patients have been operated upon too recently to report the end results.

DISCUSSION

For an understanding of inversion sprains of the ankle and their possible sequelae we must consider the anatomical arrangement of

the ligamentous apparatus investing the lateral aspect of the joint. The fibular collateral ligament consists of three bands or fasciculi (1). The posterior fasciculus or posterior talofibular ligament, the strongest of the three, running almost horizontally from the medial and back part of the fibular malleolus to the posterior surface of the talus, is rarely injured (2) and is therefore of no particular clinical interest.

The central band, the calcaneofibular ligament, is the longest of the 3, running as a narrow rounded cord from the *apex* of the fibular malleolus downward and slightly *backward* to the lateral surface of the calcaneus. The anterior fasciculus is the anterior talofibular ligament, the shortest of the three segments. It extends from the *anterior* margin of the fibular malleolus *forward* and medially to an attachment on the talus just in front of the lateral articular facet (Figs. 12 and 13).

Pipkin (8) has termed the calcaneofibular ligament the "long hinge" of the ankle and claims that this is the structure involved in serious tears of the ankle ligaments. Leonard (3) however, concluded from cadaver experiments in which the various ligaments were cut that the anterior talofibular ligament is the most important component of the fibular collateral ligament.

Since it may be observed (Fig. 13) that the calcaneofibular ligament has no significant contact with the ankle joint proper, its stabilizing action as far as the talofibular articulation is concerned can be only an indirect one. On the other hand the anterior talofibular ligament is the only structure really investing and supporting the talofibular joint where it is vulnerable to injury from inversion trauma. It should therefore be expected that symptoms referable to the fibular component of the ankle mortise after ligamentous injury should chiefly involve the anterior fasciculus and not the middle one. This would explain the consistent localization of the symptoms in our cases to a point *anterior* to the fibular malleolus. It would also offer a logical explanation for Leonard's experimental findings and would tend to disagree with Pipkin's claim regarding the relative importance of the calcaneofibular ligament.

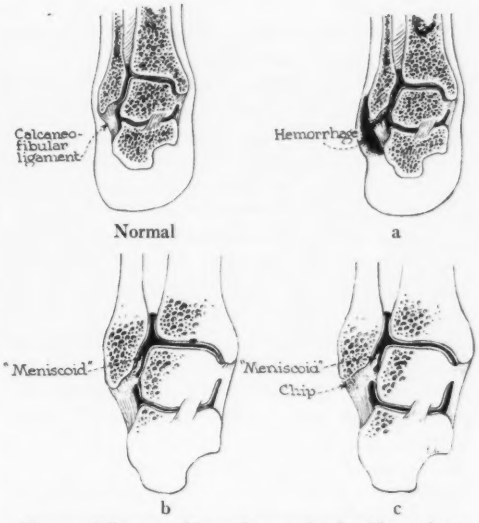


Fig. 14. Diagram of inversion sprain of ankle, with tear of ligament and synovial lining, joint exudation and hemorrhage shown in a. b, Formation of "meniscoid" following imperfect repair and absorption of effects of injury. c, Para-articular ossification of ligamentous hemorrhage.

When a patient suffers a significant inversion twist of the ankle, he has a varying degree of tearing of the anterior talofibular and calcaneofibular ligaments (2), associated with hemorrhage into the joint (Fig. 14). We believe from our surgical observations that the following changes result. The injury gives rise to a traumatic synovitis with synovial thickening and exudation. In most cases the exudate and hemorrhage are completely absorbed as repair is effected. Occasionally, however, the absorption of this material is incomplete, and a small portion of this tissue persists in the interval between the fibula and the talus, where it becomes hyalinized and molded from the pressure of the articulating bones. It is our belief that repeated pinching of this tissue is the cause of the recurrent and chronic pain and swelling in the cases described.

Furthermore, the organizing hemorrhage within the ligament may undergo ossification so that an island of bone is formed (Fig. 14c). It will be observed that this island is consistently situated within or just under the anterior talofibular ligament. The ossicle it-

self may exist, however, without pain, if it is not associated with a mass of tissue lying within the ankle mortise.

The development of a meniscoid contour of the hyalinized fibrous tissue between the talus and fibula affords an interesting anatomical speculation, especially since its location is quite analagous to that of the articular disk of the wrist.

If our concept of the ankle derangement described is valid, the most logical prophylaxis against prolonged disability after severe or moderately severe inversion sprains is the use of cast immobilization. This has been stressed frequently as a means of promoting repair of a ruptured fibular collateral ligament, in which case about 6 weeks of immobilization are required. But for sprains without evidence of ligamentous rupture or avulsion, a cast worn for 3 weeks to allow the best possible absorption of the hemorrhage and exudate should afford the best means of avoiding the development of an internal derangement which is essentially a localized traumatic arthritis of the fibular component of the ankle.

However, if we are faced with the problem of a chronically disturbed ankle, without evidence of instability of the talus or osteochondritis, occurring after an inversion sprain, we should consider that the symptoms may be due to the presence of a hyalinized connective or scar tissue mass within the ankle mortise. The term "chronic sprain" should be discarded. All reasonable conservative efforts should be made to obtain relief, but surgery is indicated for the intractable cases. We place a slightly curved vertical incision with anterior convexity, 1½ inch in length, just anterior to the distal end of the fibula. The anterior talofibular ligament and the synovial lining are incised in the same line. The inferior aspect of the talofibular articulation is exposed by a retractor placed deeply just below the tip of the fibula. If the ankle is then alternately inverted and everted, the tissue which is interposed between the fibula and talus is readily demonstrable.

SUMMARY

Persistent pain and swelling over the fibular aspect of the ankle following an inversion sprain may be due to a derangement in which a mass of hyalinized connective tissue becomes impinged between the fibula and the talus. The symptoms can be effectively relieved by simple removal of the offending tissue.

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SHOULDER GIRDLE AMPUTATION

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THE radical resection of malignant tumors is a time-honored and respected surgical principle. However, the anatomic location of such lesions is often a factor limiting the extent of their removal. Certainly this is true when an extremity is involved, for its loss by amputation in order to accomplish complete excision of a malignant growth is abhorred by patient and physician alike.

The shoulder girdle amputation, although necessarily an extremely mutilating procedure, has in certain instances a legitimate place in surgery. Occasionally it must be accepted as the only adequate method of definitive treatment for those tumors unfortunately located in areas not amenable to curative surgery of any lesser degree.

Oftentimes because of the surgeon's justifiable reluctance to suggest a necessary shoulder girdle amputation, patients are subjected to multiple inadequate local excisions of malignant lesions about the shoulder area. Two of our patients each underwent 5 inadequate surgical procedures before radical shoulder girdle amputation was performed. The recurrence of the lesion makes the interscapulothoracic amputation as inevitable as it is unwelcome. It becomes apparent that given an extensive tumor in or about the shoulder joint, a grave error can be committed if an interscapulothoracic amputation is not performed at the earliest possible moment that it appears indicated. This concept has led to an analysis of our cases, few in number with respect to those in the literature, but a significant number with respect to one institution.

In the history of the University of California Hospital, 10 patients have had interscapulothoracic amputations for malignant tumors of the shoulder girdle. One of the patients had a bone tumor. The remainder were operated upon for malignant lesions of soft tissue, as noted in Table I. As might be expected, 8 of the tumors were sarcomas while only 2 were carcinomas. The age of the patients ranged from 12 to 75 years.

There was no operative mortality in the series. Three patients died within 1 year of operation from widespread metastases (Table II). One of them, a man aged 75, had had a squamous cell carcinoma of the hand for 5 years which suddenly and rapidly metastasized to the epitrochlear and axillary lymph nodes and the adjacent soft tissue of the right shoulder region. Since no clinical or roentgenological evidence of distant metastases could be demonstrated, a shoulder girdle amputation was performed in October, 1947. However, metastatic deposits in the lungs became apparent soon after surgery. Another patient was a 26 year old white female who had a malignant melanoma of the left shoulder area with palpably enlarged cervical lymph nodes. Shoulder girdle amputation was combined with a left radical neck dissection. Although pathological study of the cervical glandular chain demonstrated no involvement by malignant cells, the patient expired 5 months after operation from the effects of widespread metastases. The third fatality was due to a melanosarcoma in a man aged 45. The lesion was metastatic in the axilla and shoulder

TABLE I.—PATHOLOGY

Case	
1	Plasmocytoma, head of humerus with soft tissue involvement
2	Recurrent fibrosarcoma with radiation ulcer and severe pain
3	Mesothelioma, left shoulder region
4	Carcinosarcoma arising in burn scar, metastatic to periaxillary tissues
5	Myxofibrosarcoma of breast, axilla, and chest wall
6	Hemangioendotheliosarcoma, right shoulder and axilla
7	Melanosarcoma metastatic to periaxillary tissues from left shoulder region
8	Melanosarcoma metastatic to periaxillary tissues from right forearm
9	Squamous cell carcinoma metastatic to periaxillary tissues from hand
10	Squamous cell carcinoma recurrent in axilla following axillary dissection

From the Division of Surgery, University of California School of Medicine, San Francisco.

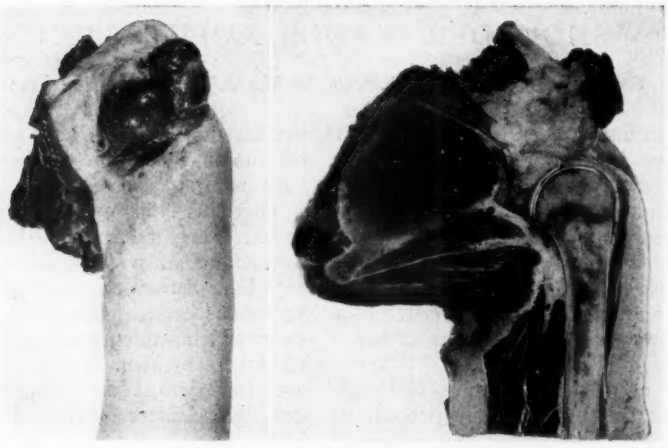

Fig. 1. Case 3. a, left. Malignant mesothelioma which recurred after each of 5 local surgical procedures and irradiation therapy. b, Note the intimate relationship of the tumor to the joint capsule.

Fig. 2. Case 4. Large fungating tumor in the region of elbow is apparent. Its rate of growth was markedly stimulated by multiple inadequate attempts at local excision.

region from a primary focus in the right forearm. Widespread metastatic deposits became apparent within 3 months after shoulder girdle amputation.

Seven patients are now living from 10 months to 34 years after operation (Table III). The earliest operation, and the only one performed prior to 1940, was performed in 1916 by Dr. Howard C. Naffziger. This patient, now living and well in Ireland, had a malignant plasmocytoma of the head of the humerus with extensive involvement of the soft tissues about the right shoulder joint.

a b c

Fig. 3. Case 5. a, The recurrent myxofibrosarcoma following radical mastectomy involved the region of the right breast and shoulder. b, Note the proximity of the tumor to the humerus and blood vessels (indicated by arrow). c, The patient is alive and well 4 years after surgery was carried out.

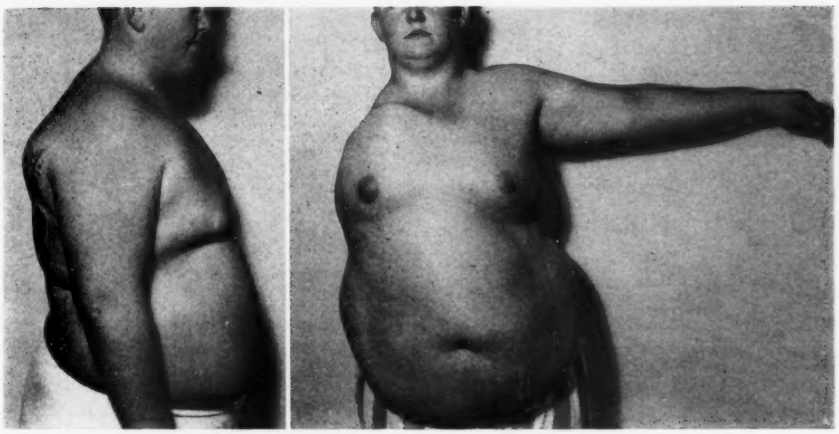

Fig. 4. Case 6. Shoulder girdle amputation provided a wide margin of resection about the several tumor deposits in the axilla and posterior scapular region. However, the lesion recurred locally in the region of the right nipple 9 months after surgery.

a b c

Fig. 5. Case 10. a, Lymphedema and marked pain resulted in almost total loss of function of the upper extremity after axillary dissection. b, and c, Note how the simple prosthesis restores the contour of the upper torso.

The ineffectiveness of less radical treatment is demonstrated by those patients who have been subjected to numerous inadequate local excisions of a malignant tumor. A 44 year old woman became addicted to morphine because of constant severe pain from chronic ulceration of the skin and ankylosis of the left shoulder joint following repeated local excisions and neutron treatment for a recurrent fibrosarcoma of the shoulder region. Shoulder girdle amputation was performed after the patient had withstood 4 years of intermittent surgery, radiation, and intense pain. There is no evidence of recurrence and the patient considers herself to be in excellent health 7 years after operation. A malignant mesothelioma (Fig. 1) in a 12 year old girl recurred after each of 5 local surgical procedures followed by irradiation therapy. The patient is well 9½ years after shoulder girdle amputation.

A man aged 48 had a rapidly growing, fungating tumor in region of the elbow (Fig. 2)

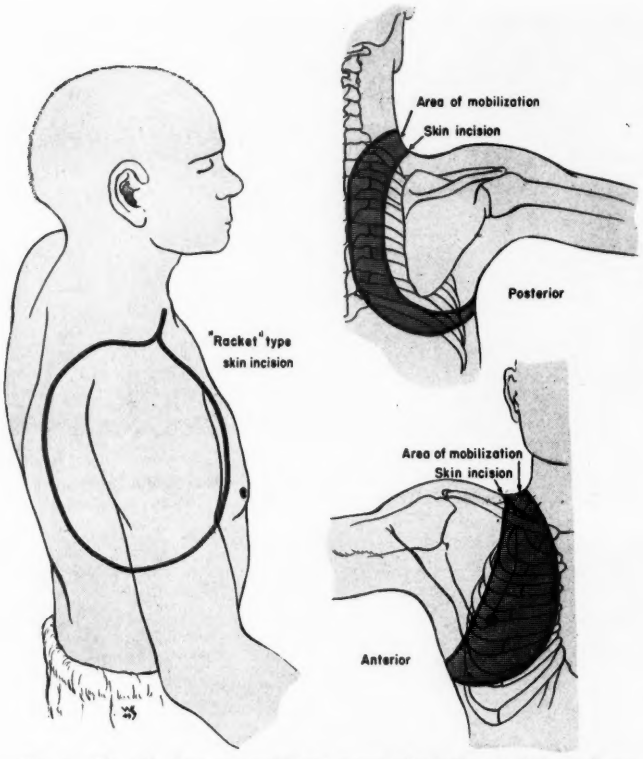

Fig. 6. The skin flaps are mobilized extensively both anteriorly and posteriorly to provide a wide margin of musculofascial resection. The racket type incision is preferred.

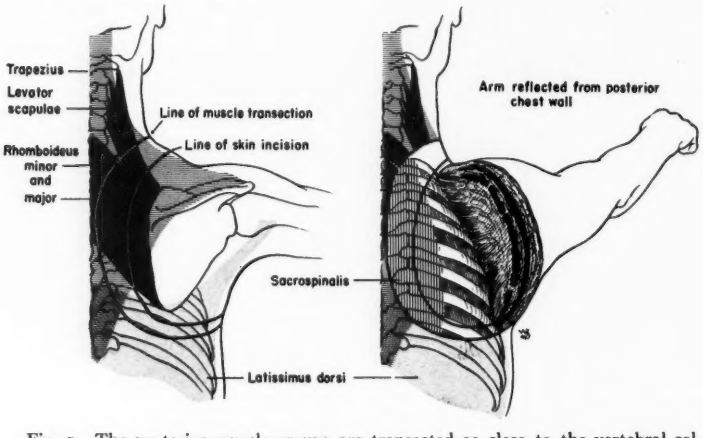

Fig. 7. The posterior muscle groups are transected as close to the vertebral column as possible. The extremity is then elevated, the plane of dissection being the chest wall.

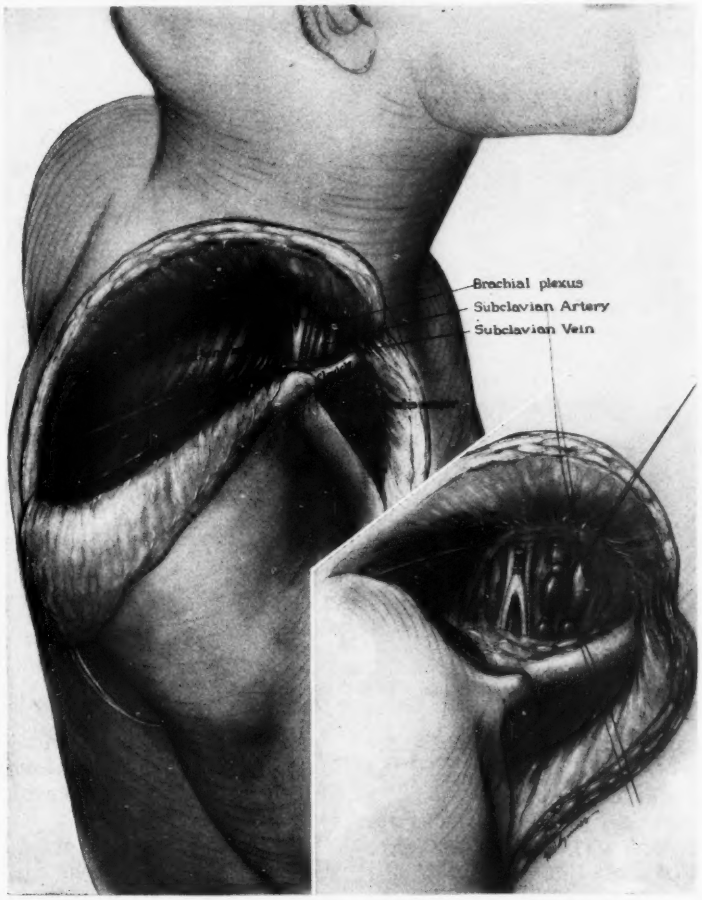

Fig. 8. With the posterior portions of the extremity elevated from the thoracic cage, the neurovascular structures can be reached from the posterior approach. This method allows for better exposure and control of the major structures. The trunks of the brachial plexus are ligated with single No. 40 cotton without injection of their stumps. The vascular structures are doubly ligated and transfixed with doubled No. 40 cotton material.

which recurred 3 times in a period of about 6 months. The pathologic diagnosis was carcinosarcoma. Shoulder girdle amputation (which the patient had once refused) was performed because of axillary involvement. Three years after operation examination reveals no evidence of recurrence of the tumor. A carcinoma of the hypopharnyx has recently appeared for which the patient is receiving radiation therapy.

A satisfactory result was obtained in a 56 year old woman with a myxofibrosarcoma which recurred 2 years after radical mastectomy. The region of the right breast and shoulder was involved by malignant tissue (Fig. 3). The patient is well 4 years after surgery.

In a 15 year old boy, an attempted local excision elsewhere of a hemangioendotheliosarcoma was unsuccessful (Fig. 4). The tumor

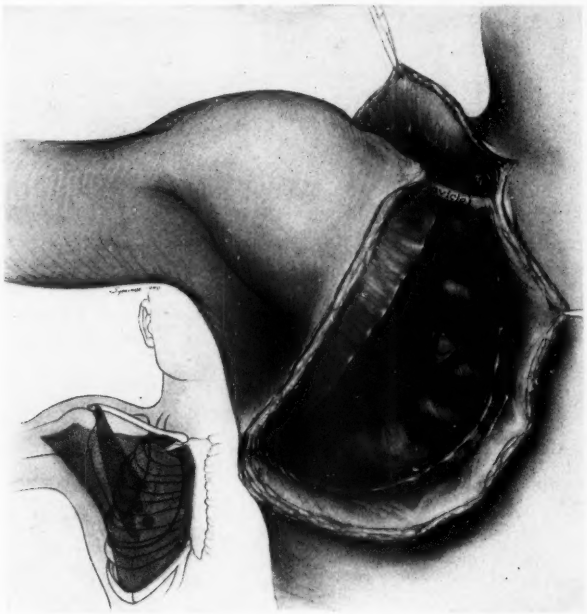

Fig. 9. The neurovascular structures have been controlled from the posterior approach. The anterior dissection divides the pectoral muscles as shown. Note that the clavicle is preserved intact until late in the operation to prevent excessive tension on the subclavian vessels.

apparently originated in the posterior scapular region and metastasized extensively to the axilla. Shoulder girdle amputation was performed but pulmonary and local metastases became evident 9 months after surgery.

A 75 year old woman had a history of a growth occurring in an old burn scar of the hand which was excised in 1936. Eight years later an axillary dissection was performed for metastatic squamous cell carcinoma. By April 1949 there was marked pain, lymphedema, and almost total loss of function of the entire upper extremity (Fig. 5), and shoulder girdle amputation was performed. A small local skin recurrence was excised 7 months after surgery. No further evidence of recurrence has appeared.

In the final analysis it must be recognized that such extensive lesions must of necessity require operative procedures of the magnitude described. It is seen also that in a significant number of patients a favorable prognosis can be expected. Moreover, these patients seem to adjust themselves to the loss of an upper extremity far more readily and easily than might be anticipated. A simple prosthesis

TABLE II.—ANALYSIS OF FATAL CASES

Case No.	Sex	Age years	Diagnosis	Procedure	Survival time	Cause of death
7	F	26	Melanosarcoma	Shoulder girdle amputation combined with radical neck dissection	5 months	Widespread melanotic metastatic deposits
8	M	45	Melanosarcoma	Shoulder girdle amputation	3 months	Widespread melanotic metastatic deposits
9	M	75	Squamous cell carcinoma	Shoulder girdle amputation	7 months	Pulmonary metastases. Carcinoma of prostate

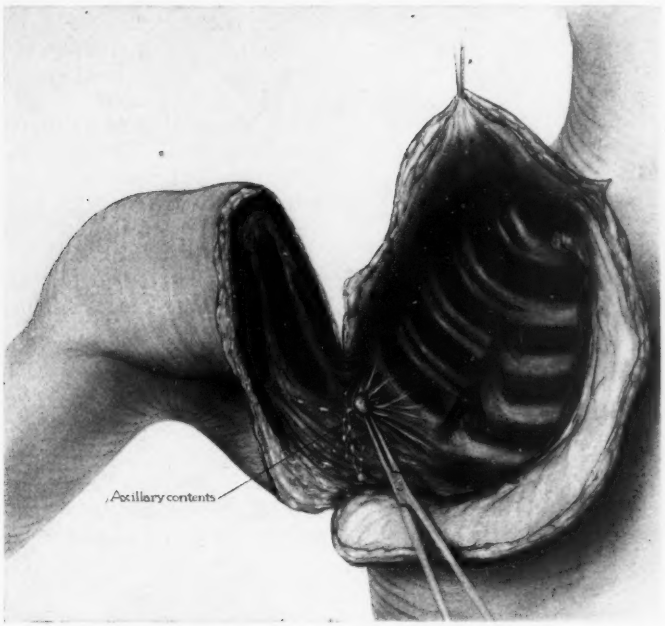

Fig. 10. After the clavicle is transected the axillary contents are swept from the chest wall by combining blunt with sharp dissection.

(Fig. 5c) can be fitted to restore the contour of the upper torso.

OPERATIVE TECHNIQUE

The patient is placed on his side and the entire involved extremity is sterilely prepared and draped so that it can be freely moved during the operation. A racket-shaped incision is made with its "handle" lying along the upper border of the clavicle, the circular portion of the incision embracing the junction of the arm with the trunk. Adequate amounts of skin for primary closure are preserved whenever possible. Skin and subcutaneous tissue flaps are fashioned posteriorly as far medially as the spine and anteriorly to the corresponding border of the sternum (Fig. 6).

The elevation of the skin flaps posteriorly exposes the trapezius, the major and minor rhomboid, and the levator scapulae muscles. These are transected near their vertebral origins with the electrosurgical knife, thereby exposing the sacrospinalis muscle group and the posterior chest wall. The severed muscle groups are reflected lateralward, and with them is carried the scapula together with its superficial and deep musculature (Fig. 7). The serratus posterior superior muscle is not disturbed.

TABLE III.—ANALYSIS OF SURVIVING CASES

Case No.	Sex	Age years	Diagnosis	Sequellae	Survival time
1	M	34	Plasmocytoma	Living and well	34 years
2	F	44	Recurrent fibrosarcoma with radiation ulcer	Living and well	7 years
3	F	12	Mesothelioma	Living and well	9½ years
4	M	48	Carcinosarcoma	No recurrence. Developed carcinoma of hypopharynx, now under radiation therapy	3 years
5	F	56	Myxofibrosarcoma of breast and axilla	Living and well	4 years
6	M	15	Hemangioendotheliosarcoma	Local and pulmonary metastases	13 mos.
10	F	75	Squamous cell carcinoma	Small skin recurrence excised 7 months after surgery	10 mos.

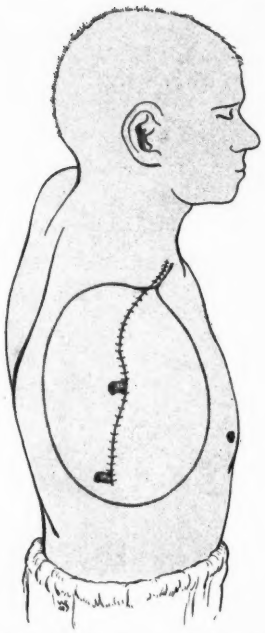

Fig. 11. There is usually ample skin for primary closure. It is wise to drain the large area of dissection. A large pressure dressing is applied.

The scapula is elevated by dividing, with blunt and sharp dissection, the areolar tissue holding it against the chest wall. The progress of the operation is directed anteriorly toward the supraclavicular space, brachial plexus, the subclavian vessels, and the clavicle. The posterior approach to these structures facilitates their identification and control and makes the attack on them more exact and less dangerous than by the anterior approach. Several approaches have been described, but we prefer the posterior one for the reason that it lessens the hazard of injury to the large blood vessels.

The trunks of the brachial plexus are divided and ligated with single No. 40 cotton ligatures close to their emergence from between the prevertebral muscle groups. The nerve stumps are not injected. The subclavian artery then comes into view and is controlled by doubled No. 40 cotton ligatures and transfixion sutures of the same material. The subclavian vein is likewise controlled (Fig. 8). The clavicle is then transected with a Gigli saw at the junction of its inner and middle thirds. Preserving the clavicle intact to this point in the operation protects the subclavian vessels and prevents injury to them by excessive traction (Fig. 9). The pectoralis major muscle is then divided near its sternal origin and the entire upper extremity is removed from the chest wall by sweeping the contents of the axilla lateralward from the thorax (Fig. 10).

Primary closure is done if possible. If this is not possible the remaining area is skin grafted. In 1 case, a full thickness graft cut from the excess tissue of the local flaps was used (Fig. 11).

DISCUSSION

Malignant lesions in and about the shoulder joint frequently can be cured by interscapulothoracic amputation. When malignant involvement of the muscular, fascial, and bony components of the shoulder region with or without extension to the axillary contents has occurred, an extensive resection of the entire upper extremity along with its attachments to the trunk must be performed. The wide removal of musculofascial planes accomplished by such a procedure provides the margin of resection necessary for the successful operative treatment of such extensive lesions. Because of the structures involved, most of the malignant tumors will arise from connective tissue anlage. As these sarcomas metastasize by way of the blood stream, the chance of recurrence is lessened by the wide removal of the vasculature in the neighborhood of the tumor thus accomplished.

It is a long established fact that the smaller the diseased part, the easier is the decision to sacrifice it. The larger the part to be excised, the greater is the tendency to delay its removal because of the effect upon the individual. However, when one is faced with a malignant growth in and about the shoulder joint, if there is the slightest prospect of a cure, the interscapulothoracic amputation should be performed. The failures attendant to treating such serious disease should not annul in the conscientious surgeon his trust in a vigorous attack upon these lesions. This is especially true of the metastatic malignant melanomas

of the shoulder region. The tendency in such cases is to grow weary of trying for the rare success. However, to do so is to deny these unfortunate individuals their only opportunity for a normal life.

CONCLUSION

The interscapulothoracic amputation has a definite place in surgery. There is the possibility that with respect to the melanosarcomas we hold too hopeful views of what is attainable by these procedures. For other types of malignant lesions involving the region of the shoulder, our observations indicate that in a significant number of cases their excision by means of radical amputation of the entire shoulder girdle is attended with favorable results.

FACTORS INFLUENCING THE PREVENTION AND CURE OF CANCER OF THE THYROID

GEORGE CRILE, JR., M.D., F.A.C.S., Cleveland, Ohio

IN recent years the reported incidence of cancer in operations performed for nontoxic nodular goiter has been so high that many surgeons have advised removal of all nontoxic nodular goiters (6). The purpose of this study is to determine (1) how frequently prophylactic operations might prevent the development of fatal cancer of the thyroid, (2) how often delay in removal of a seemingly innocuous nodule might result in death of the patient from cancer, and (3) how the prognosis is influenced by type of operation performed.

This report is based on 50 consecutive cases of cancer of the thyroid. In all cases the diagnosis has been established by microscopic examination of tissues. The classification of Crile and Hazard (4) has been followed.

RELATIONSHIP OF PROGNOSIS TO THE TYPE OF CANCER

The incidence of death from cancer is correlated closely with the degree of anaplasia and malignancy of the tumor. All 9 patients with undifferentiated carcinoma had died or had developed inoperable recurrences when last traced. Likewise all but 1 of the 5 patients with sarcomas of the thyroid were dead or had recurrences, and the 1 patient who was well 3 months after operation has not been followed longer.

In contrast to this discouraging record 25 of the 29 patients with papillary carcinomas of the thyroid and the 1 patient with an angioinvasive adenoma are alive and apparently free of recurrence from 8 months to 14 years after operation. One of the remaining died of unrelated causes and without recurrence 2 years after operation. In the only 3 patients who have died of papillary carcinoma the original cancers had been removed incompletely 4 years, 9 years, and 13 years respectively before they first consulted me with massive unremovable recurrences. Thus all of the papillary carcinomas and angioinvasive adenomas which had not been operated upon previously have been controlled by operation regardless of the extent of the cervical metastases and without resort to irradiation therapy. All of the followed patients with sarcomas and undifferentiated carcinomas, on the other hand, are dead or living with inoperable recurrences despite surgical attempts to remove the tumors and despite administration of roentgen therapy after operation.

Two of the small group of 4 patients with adenocarcinomas (malignancy of which is midway between the previous groups) are without recurrence and 2 have died of the disease.

In our experience, provided the tumors of low malignancy are treated by an adequate operation, the prognosis in thyroid cancer is closely related to the grade of malignancy.

RELATIONSHIP OF CURABILITY TO PROMPTNESS IN PERFORMING THYROIDECTOMY

The question that next arises is, "Would the rate of cure have been higher if thyroidectomy had been performed as soon as the malignant tumor was observed?" In order to answer this question the histories of the patients with incurable cancers have been analyzed.

We must disregard the 3 patients who ultimately died of recurrent papillary carcinomas

TABLE 1.—FIFTY CONSECUTIVE CASES OF CANCER OF THE THYROID

Type of cancer	No. of cases
Papillary carcinoma	29
Nonpapillary carcinoma	
Angioinvasive adenoma	1
Andenocarcinoma	4
Undifferentiated carcinoma	9
Special types	
Nonencapsulated sclerosing tumor	0
Squamous cell carcinoma	0
Metastatic carcinoma	2
Sarcoma	
Fibrosarcoma	2
Lymphosarcoma	3

From the Cleveland Clinic and the Frank E. Bunts Educational Institute.

many years after an inadequate removal of the primary tumor because information is lacking on what factors influenced the failure of the first operation or how long the goiter had been present before the first operation was performed. Two patients whose carcinomas were proved to be metastatic from the kidney and adrenal must also be disregarded because thyroidectomy could not have influenced their prognosis. This leaves a group of 15 patients with primary cancer of the thyroid all of whom have died of cancer or who had inoperable recurrences when last seen. All of these patients had undifferentiated carcinomas, sarcomas, or adenocarcinomas of high malignancy.

In 7 of these 15 cases the tumor was clearly inoperable when first observed, and only a biopsy was performed. In an additional 6 cases thyroidectomy was attempted but the tumor could not be removed completely. In only 2 cases did it appear that all the tumor was removed, but one of these patients developed a local recurrence and the other died of distant metastases.

Excluding 1 patient who had noted progressive enlargement of a goiter for 36 months, the average duration of the enlarging tumor prior to operation was only 3 months in the incurable cases. Only 2 patients had noted symptoms longer than 6 months and fewer than half had been aware of a tumor of the thyroid for more than 3 months. It is thus doubtful if earlier operation would have effected any striking increase in the curability.

There was a striking contrast between the fatal prognosis of undifferentiated tumors (regardless of how early they were removed) and the excellent outlook for patients with tumors of low grade malignancy even when operation was delayed for many years. Most of the patients with papillary carcinomas have been followed more than 5 years and many over 10 years since operation. But this group of patients gave histories of having had thyroid tumors or more often lateral cervical metastases for an average of 5 years prior to operation. In almost all of the cases it was clear that the nodule the patient identified as having been present for so long was the same nodule later found to be malignant. In the 2 surviving patients with the moderately malignant adenocarcinomas, delays of 2 years and 20 years preceding operation have been followed by apparent cures, whereas the 2 patients who died of this type of carcinoma were treated within 2 months of the onset of symptoms. These observations again emphasize that, within wide limits, the type of cancer and the type of operation performed for its removal have a greater bearing upon prognosis of patients with carcinoma of the thyroid than does the time at which the operation is performed. By this the implication is not that it is safe to defer operation for suspected malignant lesions, but rather it is intended to point out that in low grade carcinomas delay is not always disastrous nor is promptness in removal of highly malignant tumors always rewarded by cure. Undoubtedly there is a point in either type of cancer beyond which delay might be fatal or before which cure might be obtained; review of the cases in this series does not indicate that the time factor is as important as one might expect.

TABLE II.—COMPARISON OF HISTORIES OF PATIENTS SUCCESSFULLY TREATED WITH THOSE IN WHICH TREATMENT FAILED*

	Successfully treated	Treatment failed
	30 patients with no recurrence or metastasis	15 patients dead of carcinoma or living with recurrence
Average duration follow-up	4.6 years	1 year
History of recognized goiter for many years preceding development of rapidly enlarging cancer	1 patient**(?)	3 patients
History of progressive enlargement of tumor	14 patients, progressive enlargement 16 patients, no progressive enlargement	All patients noted progressive enlargement
Carcinoma probably present over 1 year preoperatively (history)	22 patients	1 patient
Probable duration of carcinoma before operation (history)	58 months (average)	5 months (average)
Histology		
Papillary carcinoma	26	0
Angioinvasive adenoma	1	0
Adenocarcinoma	2	2
Sarcoma	1***	4
Undifferentiated carcinoma	0	9

*Three patients with papillary carcinoma whose first operation was done elsewhere and 2 patients with carcinoma metastatic to thyroid excluded from this table.

**History 20 years—solitary tumor all of which was carcinoma—recent slight enlargement. Probably low grade carcinoma from the beginning.

***Followed only 3 months since operation.

In Table II the histories of the patients who have survived without recurrence are compared with those of the patients who have died or have incurable recurrences.

CONCLUSIONS TO BE DRAWN FROM COMPARISON

1. Low grade (papillary) carcinomas of the thyroid may exist for many years without enlarging or causing any symptoms other than the presence of the primary tumor and its cervical metastases.

2. Despite a long history and failure to enlarge, a firm tumor of the thyroid may be a low grade carcinoma.

3. Delay of several years in removing a low grade (papillary) carcinoma, although undesirable and possibly dangerous, does not often alter the good prognosis, provided an adequate operation is performed.

4. The low grade (papillary) carcinomas of the thyroid do not show any special tendency to develop in pre-existing goiters. The nodules probably are carcinomas from the first.

5. The highly malignant undifferentiated carcinomas and sarcomas show a definite tendency to arise in goiters large enough to have been recognized by the patient many years before the malignant tumor developed.

6. The highly malignant tumors enlarge rapidly and progressively and usually cause symptoms of sufficient severity to necessitate operation within 3 months of their onset.

7. If a tumor of the thyroid causes no symptoms and does not enlarge it is not likely to be highly malignant.

8. Early operation does not appear to alter significantly the incurability of the highly malignant tumors of the thyroid. Most of these appear incurable even when first observed.

9. There is a small group of adenocarcinomas of moderate malignancy which may behave in a variable manner, some being curable even many years after their apparent origin and others being incurable even when removed within 2 months.

VALUE OF "PROPHYLACTIC" REMOVAL OF NONTOXIC NODULAR GOITERS

Disregard of an apparently benign goiter was rarely a factor in causing death from cancer of the thyroid. Only 3 of the 15 patients with incurable cancer had noticed the presence of a goiter prior to the sudden appearance and rapid growth of the malignant tumor. The incidence of known pre-existing nodular goiter in this series is thus only 20 per cent, as compared with the 4 to 10 per cent normal expectancy of clinically detectable nodular goiter in patients of this age group in the Great Lakes area (3). Since 4 of the 15 patients with incurable cancer had noticed a goiter many years before, had disregarded an enlarging tumor of the thyroid for more than 6 months, or had neglected both a pre-existent goiter and its recent enlargement, it is possible that in these 4 cases earlier operation either might have prevented the development of cancer or have cured it in its early stages. But even assuming that subtotal thyroidectomy does give 100 per cent protection against the subsequent development of cancer, which it does not (7), and assuming that all of the patients with highly malignant tumors could have been cured had they been operated upon a few days or weeks after the onset of symptoms, which in our experience they could not, prophylactic or early thyroidectomy would at the most have prevented only about one-quarter of the deaths from cancer of the thyroid. Moreover, since approximately 4 per cent of all people and a much higher percentage of the older people in the Great Lakes area have palpable nodules in their thyroids (3), it would be necessary to remove millions of small nontoxic nodular goiters in order to effect a highly theoretical 27 per cent reduction in the incidence of incurable cancer of the thyroid. Since death from cancer of the thyroid is so rare, accounting for only 0.4 per cent of all deaths from cancer (8), prophylactic surgery performed on such a scale would be not only economically unsound but could well cause more postoperative deaths than would have occurred from cancer if the goiters had not been removed. Routine prophylactic removal of all nontoxic multinodular goiters does not therefore appear to be the sole answer to the problem of thyroid carcinoma.

RELATIONSHIP OF CANCER TO PRE-EXISTING GOITER

If benign nodules in the thyroid frequently become malignant, the chances of developing

cancer would be greatest in the more common multinodular goiters which outnumber the solitary adenomas at least 4 to 1, and each of which has 2 or more nodules capable of undergoing malignant change. Yet all evidence points to the fact that cancer is most often found in the tumors, which on the basis of the clinical examination appear to be solitary (1). Although it is impossible to prove or disprove that carcinomas commonly arise in adenomas, there is reason to believe that most of the solitary nodules which are recognized eventually as carcinomas are low grade carcinomas from the beginning. Certainly it is rare today that one can find in the substance of a carcinoma of the thyroid any trace of a benign adenoma in which the malignancy might have originated, nor does one often find in benign adenomas localized areas of frank cancer. Usually the entire tumor is either benign or malignant.

Twenty-five years ago, when Allen Graham stated that 90 per cent of the carcinomas of the thyroid originated in adenomas, the data on which he based these figures were derived from gross and histologic studies of the nonmalignant thyroid tissue rather than on the clinical history of a pre-existing goiter (5). There is no implication in Graham's statement that 90 per cent of the patients had goiters of sufficient size to be recognized clinically before development of carcinoma.

At the present time the incidence of carcinomas arising in previously recognized benign adenomatous goiters is probably lower than when Graham described it. In this series 80 per cent of the highly malignant tumors arose suddenly with no history of a recognized preexisting goiter and without warning. Histologic studies of the nonmalignant thyroid tissue would unquestionably reveal a higher incidence of benign nodular goiter, but the patients themselves were not often aware of the presence of a goiter before the cancer developed.

IMPORTANCE OF CORRECT DIAGNOSIS AND COMPLETE REMOVAL OF TUMOR.

Analysis of this series indicates that we have not been able to cure any of the patients with highly malignant tumors of the thyroid by thyroidectomy. These tumors do not take up radioactive iodine and cannot be controlled by roentgen therapy. The majority are inoperable or at least incurable when first seen by a physician regardless of the shortness of the duration of symptoms. Eighty per cent of these tumors occurred in patients who had no knowledge of a pre-existing goiter. For these reasons it is apparent that the conventional prophylactic and therapeutic measures cannot be expected to influence materially the death rates from the highly malignant thyroid tumors. If progress is to be made by established methods of treatment, it must lie in perfecting the treatment of less malignant tumors.

In 43 of the 50 cases in this series the diagnosis of cancer was made prior to operation and so recorded. In 3 additional cases cancer was suspected, raising the accuracy of diagnosis of suspected carcinomas to 92 per cent. In 4 cases, all tumors of lowest malignancy, the diagnosis was not recorded prior to operation but was established in the operating room before the specimen was examined by the pathologist. In all cases, therefore, an operation for cancer of the thyroid rather than an operation for simple goiter was done. This included a total lobectomy on the affected side. There have been no local recurrences in the thyroid area of any of the 30 tumors of low or medium malignancy.

Since tumors of low malignancy can and do recur locally if they are incompletely removed, since such recurrences may invade vital structures or metastasize distantly, and since secondary operations are always more difficult and less curative than the first one, it is important to remove the primary tumor completely at the initial operation. This cannot be done unless the surgeon plans the operation on the theory that an adenoma which warrants removal at all is one which must be removed as if it were a carcinoma. An operation for removal of a solitary nontoxic adenoma must be considered not as a prophylactic procedure designed to prevent the development of carcinoma in the adenoma, but rather as an operation to remove a possible cancer existing in the thyroid at that time.

REMOVAL OF DISCRETE ADENOMA

The majority of multinodular goiters contain no firm discrete tumors and in my experi-

ence there is little likelihood that these soft multinodular goiters are or will become malignant. But when a nontoxic adenoma is suspiciously firm and discrete it should be removed completely, regardless of whether it is enlarging, regardless of its duration, regardless of whether other nodules are palpable in the thyroid, and especially if the patient is young.

All discrete tumors, benign or malignant, should be treated as malignant and removed completely by an anatomic dissection including extracapsular ligation of the inferior thyroid artery, identification of the recurrent laryngeal nerve, and removal of the affected lobe. If a complete lobectomy is performed without identification of the nerve the incidence of injury to the recurrent nerve will be approximately 5 per cent regardless of the care with which the operation is performed. In 5 per cent of the cases the nerve courses over the posterolateral aspect of the gland in such a manner as to make it impossible to remove the lobe without injury to the nerve unless it is identified. If identified permanent injury occurs in less than 0.5 per cent of the cases (2).

Complete removal of the tumors is more important than protection of the nerve. When the nerve is not identified the temptation is strong to leave a protective layer of thyroid tissue posteriorly to avoid damage to the nerve; but if the tumor is malignant recurrence results.

As in all operations for cancer the surgeon performing the first operation has the best chance of effecting a cure. If the surgeon who operates first is not prepared to perform an operation sufficiently radical to eradicate the primary tumor he would do better to perform no operation at all. Our experience indicates that recurrence of an incompletely removed papillary carcinoma is more difficult to cure than is a primary carcinoma which has been neglected until the diagnosis of carcinoma can be made clinically. An operation for removal of a discrete adenoma of the thyroid must therefore be sufficiently radical to remove a cancer of the thyroid and should consist of an anatomical excision of the affected lobe.

SUMMARY

1. It cannot be demonstrated clinically that carcinomas of the thyroid originate as often in pre-existing benign adenomas as they appeared to 25 years ago when endemic goiter was more common.

2. "Prophylactic" removal of small soft, symptomless, multinodular goiters is of little value in the prevention of fatal cancer.

3. Firm and discrete tumors of the thyroid should be removed, not because they may develop into cancer, but because they may be cancer. If such a nodule is considered to be of sufficient importance to warrant removal, it should be removed by a complete lobectomy, as if it were a recognized carcinoma.

4. Delay in removal of low grade carcinomas, although undesirable and inadvisable, has not altered the good prognosis of the patients in this series who have been subjected to an adequate operation. Conversely, early operation, no matter how radical, has not affected the uniformly poor prognosis of the patients with highly malignant tumors.

5. If all suspiciously firm and discrete nodules in the thyroid were removed as completely as if they were known to be carcinomas, the rate of cure of cancer of the thyroid could be increased.

6. Surgeons are urged to consider thyroidectomy not as a prophylactic operation designed to prevent the ultimate development of cancer, but rather as a therapeutic measure designed to eradicate existing cancer in the selected nodules that are considered suspicious of cancer.

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THE RESULTS OF SURGICAL TREATMENT OF CANCER OF THE BREAST THROUGHOUT A PERIOD OF FORTY YEARS

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DURING the forty year period between July 1907 and July 1947, the writer operated upon 156 patients with cancer of the breast. All but 4 of these patients have been traced either to the date and cause of death or to the condition present as of January, 1949 or later. In all but Case 40, the operations were typical complete excisions including removal of the pectoral muscles and axillary lymph nodes. In all but 4 cases of grossly advanced lesions, microscopic studies were made of the primary tumor and the lymph nodes. All sections were graded as to malignancy.

Fifty-six of these patients were operated upon during the period between 1907 and 1926, and the results obtained up to June, 1927[1], have been reported previously. These cases were again traced to January, 1934[2], and reported. They are here included along with the additional cases in which operations were performed up to January, 1947.

The present cases have been classified into three groups corresponding to the classification adopted by the Departmental Committee on Cancer of the British Ministry of Health.

Group I contains cases from Class 1 of the British classification, i.e., cases in which, so far as could be ascertained, the growth was entirely confined to the breast; the axillary glands were not invaded.

Group II contains cases from Class 2 in which the axillary glands were already invaded at the time of the operation, but in which there was no evidence of involvement of any other contiguous or distant organ or tissue.

Group III contains cases from Class 3 in which either adjacent or distant organs or tissues were involved, as the pectoral muscles, the skin when ulcerated, the cervical glands, or the opposite breast.

[1]The postoperative prognosis of cancer of the breast. Arch. Surg. 1928, 16: 879–886.

[2]The postoperative prognosis of cancer of the breast. Arch. Surg., 1935, 30: 629–634.

CLASS 1 CASES

Sixty-four (41 per cent) of the cases in this series were classified as Class 1. Thirty-three (51 per cent) of these patients operated upon before axillary metastases were demonstrable have died of recurrences as follows (Chart 1[3]): 1 patient died 9 months after operation, 6 died from 1½ to 3 years after operation, 9 died between 3 and 5 years after operation, 8 died during the 6th postoperative year, 4 died between 6 and 8 years after operation, 1 died 8 years and 9 months after operation, 1 died 11 years and 6 months after operation, 1 died 15 years and 6 months after operation, 1 died 24 years after operation, and 1 died 25 years after operation.

Only 16 of the Class 1 patients who died of recurrent cancer lived less than 5 years. Seventeen died in the period of from 5½ to 25 years after operation. The total survival period of these 33 patients who died of recurrences was 206 years, or an average of 6 years and 3 months. This period is significantly longer than the average expectancy for patients not operated upon and would seem to justify the assumption that, at least in the patients surviving for the longer periods, the operation served to prolong their lives.

Eleven patients have died of causes other than cancer. Four died within 3 years after operation. In the 7 other cases, the postoperative survival periods were 6 years 6 months, 8 years 9 months, 8 years 9 months, 9 years 3 months, 13 years 3 months, 18 years

[3]Charts 1 to 6 show the postoperative period of survival in black and the known preoperative existence of the tumor is represented by the space between 0 and the beginning of the black line. Thus, Case 35A had known that she had her tumor for 1 year before she came to operation and she survived 3¼ years after operation.

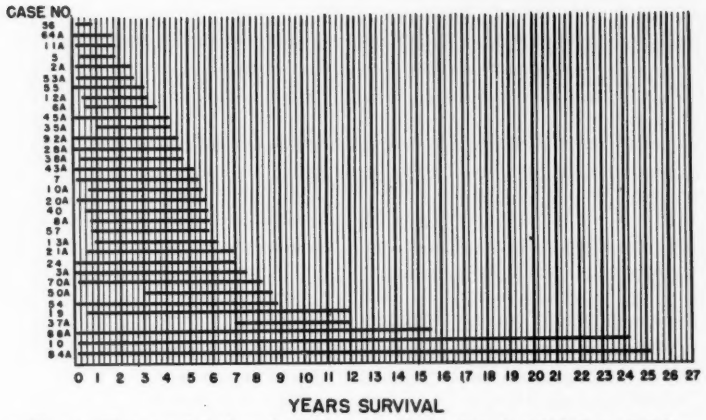

Chart 1. Shows period of survival after operation and total period of survival from time of discovery of tumor to death in patients in Class 1 who died of recurrence of tumor.

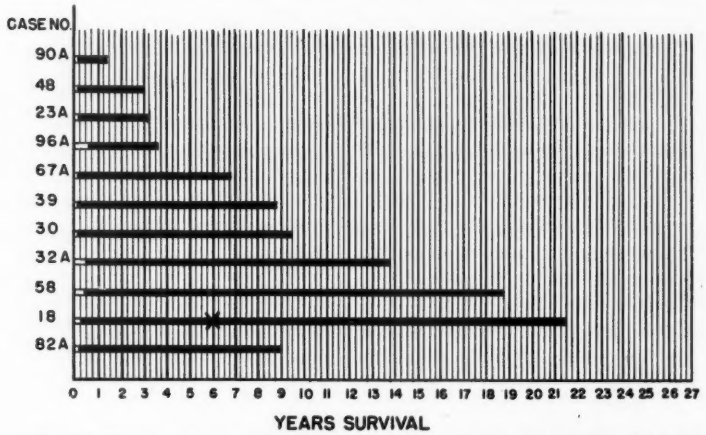

Chart 2. Shows period of survival after operation and total period of survival from time of discovery of tumor to death in patients in Class 1 who died of causes other than cancer.

4 months, and 21 years 3 months. The total survival period from the date of discovery of the tumor to the date of death in these cases was 92 years and 3 months, or an average survival period of 8 years and 4 months. The cause of death in each of these cases was definitely not cancer and in no case was there any evidence of recurrence at the time of death.

Twenty patients in Class 1 were living and free from demonstrable recurrences in January, 1949 or later. Only 2 of these patients had been operated upon less than 5 years earlier. The cancer free survival period in the remaining patients was as follows: one 5 years 10 months, one 8 years, one 9 years, one 10 years, two 11 years, one 13 years, three 14 years, two 16 years, one 18 years, one 19 years, one 20 years, one 28 years, one 30 years, and one 35 years. These 20 patients have already survived a total of 303 years since their tumors were first discovered, or an average of 15 years each, and, since to date there is no evidence of recurrence, many more

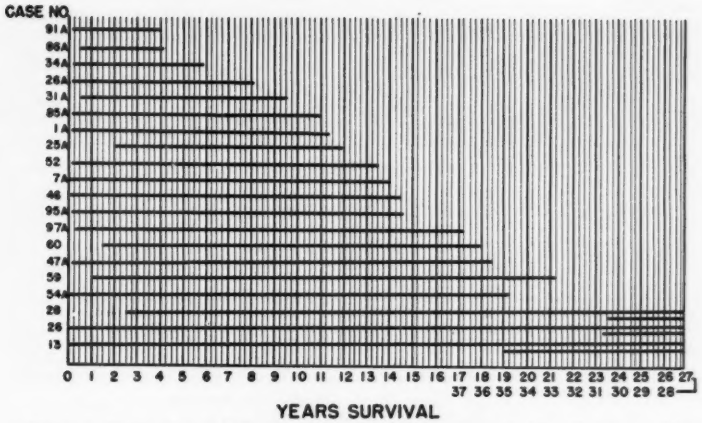

Chart 3. Shows the period of survival since operation and since discovery of tumor in patients in Class 1 living as of January, 1949.

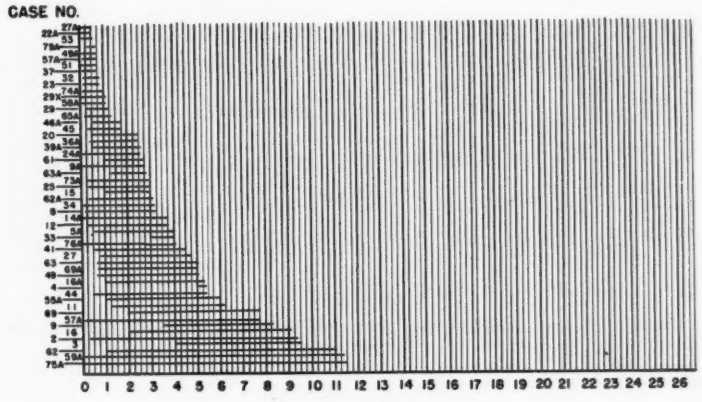

Chart 4. Shows period of survival after operation and total period of survival from time of discovery of tumor to death in patients in Class 2 who died of recurrence.

years will undoubtedly be added to their survival periods. These figures undoubtedly demonstrate that in a considerable portion of the individual patients in this group, life has been decidedly prolonged by operation. However, one should not be unreservedly generous in ascribing these results to surgery. These survivors represent the pick of the 156 cases as regards long term survival. The group is noteworthy in that more than one-third of these patients failed to report for operation until from 3 months to 2½ years had elapsed after the discovery of their tumors. These most certainly were not early cases as the term is understood when urging patients to report promptly when a lump in the breast is discovered. Case 28 will serve to illustrate this point. Although this patient had put off reporting to a surgeon for 2½ years after discovery of her tumor, hers was still an early case from the pathologist's viewpoint. This fact is almost prima-facie evidence that this was one of those slow growing tumors that may persist 20 or more years before causing death.

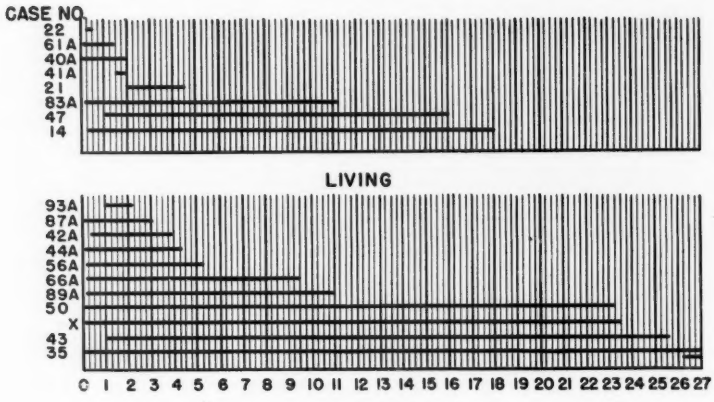

Chart 5. Shows period of survival after operation and total period of survival from time of discovery of tumor to death in patients in Class 2 who died of causes other than cancer (above); and who were living as of January, 1949 (below).

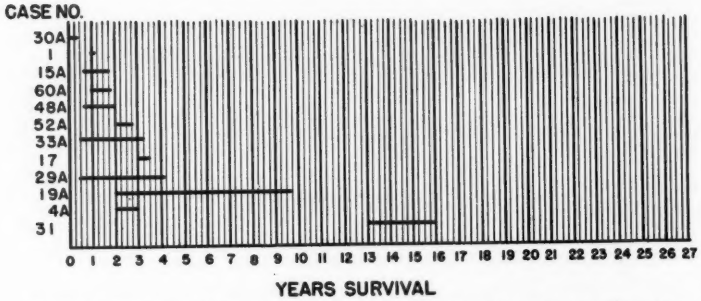

Chart 6. Shows period of survival after operation and total period of survival from time of discovery of tumor to death in patients in Class 3 all dead of cancer.

CLASS 2 CASES

Seventy-three patients (47 per cent) of this series were found to have axillary metastases without demonstrable involvement elsewhere and are, therefore, classified as Class 2 cases. Fifty-four (74 per cent) have since died of recurrent cancer.

In contrast to the Class 1 cases in which more than half of the deaths from recurrences have occurred more than 5 years after operation, we find that in the Class 2 cases 46 (85 per cent) of the 54 deaths from recurrences have occurred during the first 5 years after operation. Fourteen of these 46 patients died from 5 months to 1 year following operation. Nine of these deaths during the first postoperative year were of patients who came to operation within from 1 to 14 days after the discovery of the tumor. On the other hand, 1 patient had delayed operation 3 months, one 3 years, and one 5 years. Only 6 of the 32 patients who died from 1 to 5 years after operation were operated upon within a month of the time their tumor was first discovered. Only 8 deaths (15 per cent) have occurred after the fifth postoperative year. These 8 deaths have occurred as follows: 1 death at each of the following periods—5 years 6 months, 5 years 9 months, 7 years 1 month, 7 years 8 months, 9 years, 10 years, 11 years 4 months, and 11 years 6 months.

Eight patients in Class 2 have died of causes other than cancer. Five of these patients died within 2½ years of operation. Three, how-

ever, far exceeded the 5 year mark. One died 11 years after operation, 1 died 15 years after operation, and 1 died just short of 18 years after operation.

Eleven patients were living and apparently free from recurrences in January, 1949 or later. The postoperative survival periods in these cases up to January, 1949 were as follows: 1 year 4 months, 3 years 1 month, 3 years 7 months, 4 years 3 months, 9 years 4 months, 10 years 10 months, 23 years 3 months, 23 years 6 months, 24 years 4 months, and 27 years 9 months.

The total survival time from the date of discovery of tumors to the date of death in the 54 patients who died of recurrences was 211 years, or an average of 3 years and 11 months, which is not significantly different from what might be expected had these patients never been operated upon.

On the other hand, the average survival time of patients in Class 2 who died of other causes and those still living was 10 years and 3 months. This is apparently a significant extension of life beyond the time which might have been predicted had these patients not been operated upon. This conclusion seems particularly applicable to 8 patients in this group who survived for periods of from 10 to more than 27 years. Although each patient was operated upon promptly following the discovery of the tumor, axillary metastases were nevertheless already present, indicating a relatively high grade of malignancy in these cases.

CLASS 3 CASES

Fifteen patients were classified as Class 3 cases. Included in this group are 3 patients operated upon for local recurrences following local excisions of breast tumors by other operators. Only 1 patient in this group lived over 4 years (7 years 8 months) after operation. In 12, the tumors were obviously highly malignant and the total period of survival from date of discovery of the tumor to death ranged in these 12 cases from 5½ months to 4 years. However, if we combine preoperative and postoperative time, 1 patient survived for a total period of 7 years and 10 months, 1 patient survived 9 years and 9 months, and 1 patient not operated upon until 13 years after the development of cancer lived another 3 years after operation or for a total period of 16 years. Some authors have advised against operating upon any of these patients in Class 3. Although more often than not I have refused to operate upon patients in this group, in about half of those operated upon I would estimate that the relief afforded justified the operation.

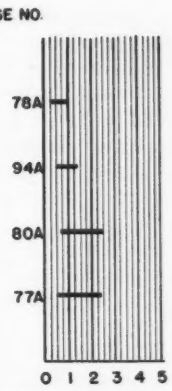

Chart 7. Shows known period of survival in cases not completely traced. Case 78A, operated upon January 4, 1926, had a very extensive rapidly growing tumor and is presumed to have died within 1 year. Case 94A, operated upon October 22, 1934, Class 3 at 5 months was in poor health when last heard from. Case 80A, operated upon June 3, 1941, was O.K. when last heard from; no record of death in State department. Case 77A, operated upon February 17, 1927, was O.K. when last heard from.

EVALUATION OF STUDY

As data have accumulated in the course of this study, several possible deductions have seemed worthy of consideration. First, the concept of malignancy as an attribute primarily of the invading cells themselves and quite irrespective of the soil furnished by the invaded host seems inadequate to explain the facts observed in the cases under study.

With very few exceptions, all of the breast cancers comprising this study were graded as to relative malignancy according to histologic concepts. Actually there was no significant correlation between the predictions based on the cell pictures and the actual long time outcome of the case. The histological picture does seem to indicate the rate of tumor cell

growth at the moment when the tumor is removed, but the clinical outcome would appear to represent the long time product of the tendency of the tumor cells to multiply, plus some restraining influence on the part of the host. By postulating the existence under some circumstances of a fairly adequate restraining factor on the part of the host it is possible to explain not only the lack of correlation between the histological pictures and the actual end results, but it helps also to explain certain other definitely observable facts. Cases 19, 88A, 10, and 84A in the Class 1 group are examples of definitely malignant tumor cells remaining dormant or having been held dormant or in check by the host for periods ranging from 10 to 21, or more years. Cases 59A and 75A in Class 2 are additional examples of the same type.

Throughout the years the occasional regression of definitely malignant tumors has been reported by many observers. In Case 2 in the Class 2 group the patient was operated upon 4 months after the tumor was first discovered. Fifteen months after operation she presented with multiple recurrent nodules scattered over the chest. Her case looked hopeless. She received 6 treatments with an old static type x-ray machine. Sometime later the multiple skin nodules began to regress and this woman remained free from demonstrable cancer for more than 7 years. Nine years after her operation she died of a rapidly progressing recurrence. Possibly the minute dosage of x-rays affected the regression. Something held this cancer in check for a long period of time.

SUMMARY AND CONCLUSIONS

Many readers may feel that the writer has overemphasized the part played by resistance on the part of the patient as a factor in the postoperative prognosis of cancer. Nevertheless, the final outcome in a number of cases in this series and especially in those recurring after many years of apparent quiescence is difficult to explain otherwise. This phase of the cancer problem has had only scant study to date. Its importance is being more and more emphasized as long time follow up records become available.

The present study indicates that a prognosis based on the histology of the tumor removed at operation has had little relation to the actual outcome in individual cases. On the other hand, it is quite evident that in a considerable proportion of cases by the time the operation is completed, the surgeon has at hand data from which he can formulate a fairly accurate prognosis. In those patients coming to operation within a few days of the discovery of the tumor with no lymph node involvement, the prognosis must remain very much in doubt. If lymph node metastasis is already present, the prognosis is generally unfavorable. On the other hand, the longer the tumor has been present without lymph node metastasis the more likely is the prognosis to be favorable. Likewise, in the Class 2 cases, the preoperative rapidity of growth, both as regards the primary tumor and the lymph node involvement, gives a fairly accurate index by which the surgeon can estimate the postoperative prognosis.

BENIGN MESOTHELIOMAS (ADENOMATOID TUMORS) OF THE GENITAL TRACT

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A RARE and interesting neoplasm occurs in the epididymis, spermatic cord, and testicular tunics of the male, and in the uterus, fallopian tube, and ovary of the female genital tract. Variously designated in the literature, this tumor, which we consider is a mesothelioma, has presented a challenge to the pathologist and the clinician. Although this neoplasm is now accepted as an oncologic entity, quantitative variation of the histologic components has led to diverse opinions regarding its histogenesis. A review of the literature and a clinicopathologic study of 35 cases of mesothelioma of the genital tract from the records of the Mayo Clinic are presented. In 4 of the 35 cases, material was sent to the clinic for evaluation.

LITERATURE

To Sakaguchi, in 1916, goes credit for describing the first mesothelioma of the male genital tract, an epididymal tumor, which he termed "adenomyoma." There followed reports of this neoplasm occurring in the epididymis and testicular tunics, published under such diagnoses as fibromyoma (41), low grade adenocarcinoma (22), lymphangioma (8, 18, 25, 31, 32, 35, 39), mixed tumor (42), adenomyofibroma (16, 17), pseudotumor (26), adenoma (5, 20), and mixed leiomyoma and lymphangioma (21, 24).

Masson, Riopelle and Simard, in 1942, were the first to report the occurrence of this neoplasm in the genital tracts of both males and females, and described cases in which this type of tumor occurred in the uterus, spermatic cord, epididymis, and tunica vaginalis. These authors also were the first to designate the lesion as "mesothelioma." Independently, in 1943, Evans (13, 14) made similar observations in regard to location and designation of such neoplasms.

Fifteen cases of adenomatoid tumors of the genital tract were reported by Golden and Ash. This, the largest reported series, included tumors located in the epididymis, testicular tunics, and fallopian tubes. Morehead designated such neoplasms occurring in the epididymis, fallopian tube, and ovary as "angiomatoid formations." Recent cases of mesotheliomas of the male genital tract reported or mentioned in the literature (3, 4, 6, 9, 12, 23, 33, 36) bring the total to 64. Certain cases of epididymal tumors reported from the Mayo Clinic in 1936 (43) and considered then to be low grade adenocarcinoma, lymphangioma, hemangioma, and angioma with endothelial hyperplasia, are included in our study.

Rare examples of uterine mesotheliomas are described in the literature. In addition to those previously mentioned, von Meyenburg described a benign cystadenomatous fibromyoma. Curtis described lymphangiectatic myomas as the result of degenerative change in uterine fibromyomas.

Prior to Evans' publication (14), the occasional mesothelioma of the fallopian tube was termed "lymphangioma." Sanes and Warner, in 1939, analyzed 17 cases previously reported and added 1 case. Connally described 1 tubal tumor as a mesonephroma, and Ragins and Crane reported 3 cases of adenomatoid tumors of the fallopian tube.

The ovary apparently is the least frequent site of a mesothelioma. Morehead reported a case of a diffuse lesion of the ovary. The 4 ovarian tumors considered as lymphangiomas by Siddall and Clinton may have represented mesotheliomas. Ashworth stated that he had seen only 1 adenomatoid tumor of the genital

Abridgment of thesis submitted by Dr. Lee to the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery, with additions.

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tract, found incidentally in an ovary at necropsy.

MATERIALS AND METHODS

Clinical and pathologic material of the Mayo Clinic, from January 1, 1910, to January 16, 1950, included 35 cases of mesothelioma of the genital tract. These neoplasms originally had been diagnosed variously. Only surgical cases were studied.

Gross specimens, preserved in formalin, were examined. Sections of representative blocks of frozen tissue were cut 10 microns thick and stained with hematoxylin and eosin. In 16 cases, sections made by paraffin block technique, cut at a thickness of 8 microns and stained with hematoxylin and eosin, also were studied. In more recent cases the tumors had been seen at the time of operation by one or more of us and studied in the fresh state grossly and by means of fresh frozen sections stained with polychrome methylene blue. Also employed were the Dresbach modification of Mayer's mucicarmine stain, Bauer-Feulgen's glycogen stain, Sudan IV stain for fat, elastin-van Gieson stain, Gömöri reticulum stain and Mallory-Heidenhain (Krichkesky's modification) stain.

In 100 cases a pathologic study was made of tumors which appeared similar to uterine fibromyomas, which had been removed surgically between June 22, 1948, and October 13, 1948, to investigate the possibility that in some cases mesotheliomas of the uterus were not being diagnosed. Four hundred and thirty-seven tumors were examined grossly and microscopically in the fresh state; of these, 228 were subserous, 188 were intramural, and 21 were submucous.

An additional study was made of peritoneum on the posterior surface of the uterus, the commonest site of uterine mesothelioma. In 25 cases the uteri did not contain fibromyomas; in 12 cases the uteri contained fibromyomas not located on the posterior surface. The overlying peritoneum in each of the 228 subserous tumors was studied microscopically.

MESOTHELIOMA OF THE EPIDIDYMIS AND TESTICULAR TUNICS

We wish to summarize data in 20 cases of mesothelioma of the male genital tract (18 affecting the epididymis, 1 the tunica albuginea and 1 the tunica vaginalis). A complete survey of all tumors of the epididymis and testicular tunics has not been made recently at the clinic, and an accurate figure representing the incidence of mesotheliomas among neoplasms occurring in this location cannot be stated. The rarity of the lesion is evident by the fact that of more than 800,000 new registrations of males at the clinic, only 17 patients were seen who had mesotheliomas.

Clinical features. Information was available in 19 of the 20 cases. The patients' ages at the time of operation ranged from 27 to 61 years; 11 patients (58 per cent of 19) were in the fifth or sixth decade of life. One patient was a negro, the others were of the white race. Thirteen patients (68 per cent) sought medical attention because of the presence of an intrascrotal tumor; 2 patients were aware of the tumor's presence but came because of an unrelated condition; 4 patients were found to have neoplasms on routine physical examination. The known duration of the tumor varied widely; usually it had been present several years, and in 1 instance the neoplasm had existed 16 years. Growth of the tumor usually was slow and progressive. Two patients had recent acute swelling. A history of trauma was given by 5 patients but it was not felt to be etiologically significant. Twelve patients (63 per cent) had had intrascrotal pain of varying intensity. Genitourinary infection was present in only 2 cases. Syphilis was not present and results of laboratory tests and roentgenograms were not significant.

Typically, a small, firm, round nodule was found in the scrotum on physical examination. Usually this tumor was felt to be located in the epididymis, but delineation from the testes could not be ascertained in 4 cases (21 per cent). The neoplasm, always single, occurred on the right side eleven times (58 per cent) and on the left, eight times (42 per cent). In 15 instances (79 per cent) the tumor was located in the region of the tail of the epididymis, in 2 cases in the head of the epididymis, and in 2 cases the exact location was not cited. A hydrocele on the side of the tumor was present in 3 cases and bilateral hydroceles were found in 2 cases; the total incidence of

associated hydroceles was 26 per cent. In no instance was the presence of metastasis evident clinically.

The most frequent preoperative diagnosis was a tumor of the epididymis or testis; whether it was considered to be benign or malignant usually was not stated. An inflammatory process, probably tuberculous epididymitis, was considered a possibility in 9 cases (47 per cent).

Simple excision of the tumor was performed in 9 cases (47 per cent), partial or total epididymectomy in 4 cases (21 per cent) and primary removal of the scrotal contents on the side of the lesion in 4 cases (21 per cent). In 2 cases the nodule was excised, a diagnosis of low grade adenocarcinoma was made with the aid of frozen sections, and orchidectomy was then performed on the side involved. Roentgen therapy was given to 2 patients postoperatively, once after simple excision and once after excision of the tumor followed by orchidectomy.

Pathologic features. Data with regard to macroscopic examination of the tumor were available in 19 cases. The tumors varied in size from 0.7 centimeter in diameter to 4 by 3½ by 3½ centimeters (Fig. 1). The diameters of 14 tumors (74 per cent) were 2.5 centimeters or less. Each neoplasm was firm, solid, and circumscribed. On cut section the surface was smooth or showed fine trabeculation and varied from grayish white to grayish yellow in color. Some tumors bulged on being sectioned.

Microscopic examination was made on 20 mesotheliomas. Wide quantitative variation appeared in different tumors and in different areas of the same tumor, but characteristic features were present in each. Fibromuscular capsules encased the tumors, definite in some cases and poorly defined in others. The surrounding tissue was not invaded. The fibrous stroma varied from a loose network to dense hyalinized tissue. Smooth muscle was found in every case, usually in small quantities located at the periphery of the tumor, but in 3 instances the muscle predominated in some areas and was present throughout. With one exception, blood vessels were infrequent within the tumor.

Scattered in the stroma were numerous spaces and groups of cells which varied widely in size, shape, and type. The pattern could be classified into 3 general types: (1) canalicular (Fig. 2), with large, "vascular" spaces lined, with flattened but not spindling cells; (2) tubular (Fig. 3), having glandlike spaces with epithelium-like cuboidal or low columnar lining cells; and (3) plexiform (Fig. 4), with solid strands and nests of cuboidal epithelioid cells. Though the tumors can be classified according to the predominant pattern present, all types were seen in each case and cells of different sizes were found lining the same space. Within acidophilic cytoplasm there was a large, oval, moderately vesicular nucleus with a single nucleolus. No mitotic figures were present. A single layer of cells lined the spaces, without true basement membrane or cilia. The lining cells differed from the endothelium in adjacent blood vessels and from the epididymal epithelium. Particularly in the canalicular pattern, cytoplasmic strands were seen in some spaces. An occasional desquamated lining cell or mononucleated cell was seen in the otherwise empty spaces. Abundant intracytoplasmic vacuoles were characteristic. Fusion of vacuolated cells was noted which seemed to form spaces. Continuity was not seen between the cells which lined the spaces and those of the tunica vaginalis.

Lymphoid cells were present in the stroma, chiefly toward the periphery of the tumor. Nodular groups of lymphoid cells could always be found, but in 2 instances only were secondary centers seen. In the 2 cases in which the patients gave histories of recent acute swelling, portions of the tumors were necrotic; in both cases subacute epididymitis was associated.

Material in the vacuoles and in the spaces inconstantly stained weakly with mucicarmine. Results of stains for glycogen and fat were negative. Few fibers of elastic tissue were noted. Van Gieson's stain confirmed the presence and distribution of smooth muscle and connective tissue. Reticular fibers formed a network of strands between the spaces. The Mallory-Heidenhain stain, which colors the cells of tubules of the kidney red, was negative in these cases.

Prognosis. The postoperative course was uneventful in every case. Subsequent history was obtained in 15 cases. The period of follow-up after operation varied from 6 months to 30 years; in 7 cases (35 per cent) the condition of the patient was followed for more than 10 years. The neoplasm did not recur in any instance and there was no evidence of metastasis.

MESOTHELIOMA OF THE UTERUS

It is considered significant that all 12 uterine mesotheliomas have been found during the past 7 years, for during this period tumors of the uterus with gross appearance of fibromyomas have been subjected to more careful scrutiny than formerly. In the 7 year period, 1943 to 1949 inclusive, over 8,000 hysterectomies were performed at the clinic; our study disclosed 10 cases of mesothelioma found at the time of hysterectomy, a relative incidence of slightly more than 1 mesothelioma to each 1,000 hysterectomies. In the same period more than 300 myomectomies were performed; 2 cases of mesothelioma were found in this group, a relative incidence of about 6 to 1,000.

Clinical features. The ages of the women ranged from 28 to 59 years; 6 were in the fifth decade of life. All 12 patients were of the white race; 5 women were nulliparas, 3 of whom were unmarried. Only 1 tumor occurred in the case of a woman who was past the menopause and this patient was asymptomatic. Symptoms such as dysmenorrhea, menometrorrhagia, lower abdominal discomfort, and diarrhea caused the other patients to seek medical attention. Three patients gave histories of pelvic infection.

Physical examination revealed that 9 patients had pelvic tumors. One patient had a retroverted uterus and right adnexal tenderness. Pelvic examination of 2 patients did not reveal any abnormal pathologic findings; one of these patients had a rectal carcinoma. Laboratory tests and roentgenograms were noncontributory. Results of all tests for syphilis were negative.

A preoperative diagnosis of uterine fibromyomas was made in 6 cases. Other preoperative diagnoses which led to surgical intervention were dysmenorrhea, menometrorrhagia and right adnexal tumor. Abdominal or vaginal hysterectomy was performed in 10 cases, in 1 case incidental to low anterior resection for rectal carcinoma. Two patients, both 28 years of age, underwent local excision of the mesothelioma. Roentgen therapy to the abdomen was employed in 1 case for an associated carcinoma of the uterine fundus.

Pathologic features. Macroscopically these tumors varied in size from 5 millimeters in diameter to 3 by 3 by 2.5 centimeters (Fig. 5). The average tumor was rounded and measured 2 centimeters in diameter. Every lesion was single and subperitoneal. Ten neoplasms (83 per cent) were located on the posterior aspect of the uterus and 2 on the anterior surface.

The tumors appeared similar grossly to uterine fibromyomas, but certain differentiating features were noted. They were solid and circumscribed but not encapsulated. On cut section the surface bulged but not to the extent usually seen in fibromyomas. The tumors were yellower than the usual fibromyoma. In 1 instance an outer zone 5 millimeters in diameter appeared to be yellower as contrasted with the rest of the tumor which was gray. Ten tumors were homogeneous in appearance; the cut surface appeared slightly mucoid and showed fine trabeculation. The peritoneal surface was smooth. One neoplasm, not a discrete tumor, occurred as an irregular area 3 by 2 by 2 centimeters on the posterior surface of the uterus.

In 9 instances (75 per cent) the mesothelioma was associated with 1 or more uterine fibromyomas. Other associated pathologic conditions in the pelvis were adenocarcinoma of the uterine fundus, subinvolution of the uterus, retroversion of the uterus, hydrosalpinx, subacute and chronic salpingitis, endometriosis, ovarian dermoid cyst, and rectal carcinoma.

Microscopically mesotheliomas of the uterus were essentially the same as tumors from the male genital tract, with certain variations. All 3 patterns occurred, but only canalicular and tubular types predominated. In 1 instance all glandlike spaces were found in fibrous stroma forming a subserosal peripheral layer (Fig. 6); smooth muscle was not found in this zone, and no spaces were scattered

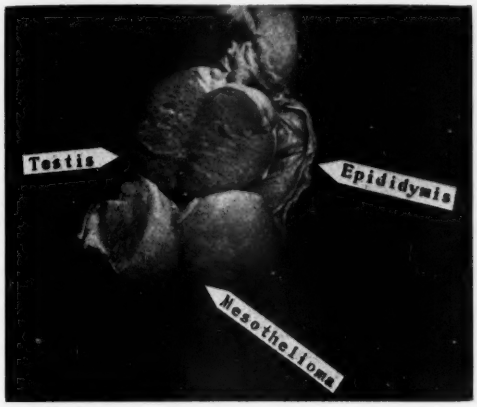

Fig. 1. Mesothelioma of the epididymis. Note relationship to the testis and epididymis. The tumor measured 3.5 by 3.5 by 3 centimeters.

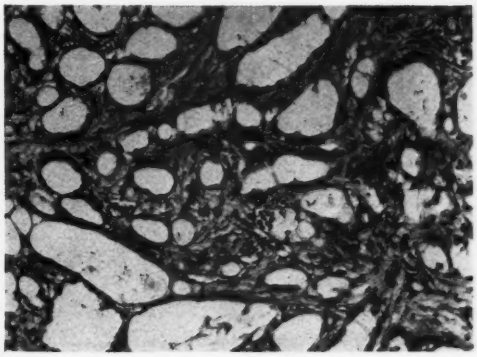

Fig. 2. Mesothelioma of the epididymis in which the canalicular pattern shows large and small spaces lined by flattened cells; the coalescing intracytoplasmic vacuoles form the spaces and scattered lymphocytic infiltration is evident (hematoxylin and eosin, ×130).

through the muscle composing the rest of the tumor. There appeared to be continuity between cells lining the spaces and those of the overlying peritoneum in one area. The other tumors were composed predominantly of smooth muscle with the characteristic tumor spaces and cells scattered throughout in varying quantities in fibrous stroma between the muscle (Fig. 7). Invasion of the surrounding myometrium did not occur. In 2 other instances there appeared to be continuity between the cells lining the spaces and those of the peritoneum (Fig. 8). In an additional tumor the cells of the peritoneum over the neoplasm were similar to those lining the spaces, but no communication was demonstrated. In the same case, a small area of adenomyomatous tissue was found in the mesothelioma; adenomyosis was present elsewhere in the uterus and no relationship of the endometrium-like cells to those of the mesothelioma was observed. In the case in which there was no discrete tumor the mesotheliomatous tissue was overlaid in part by an area of endometriosis, and endometriosis occurred elsewhere in the pelvis. The results of special stains were simi-

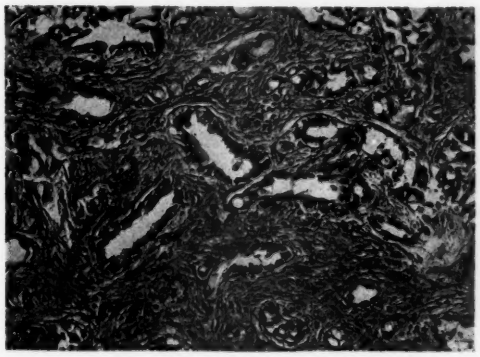

Fig. 3. Mesothelioma of the epididymis which shows predominantly the tubular pattern with glandlike spaces and cuboidal and low-columnar lining cells in a fibrous stroma (hematoxylin and eosin, ×130).

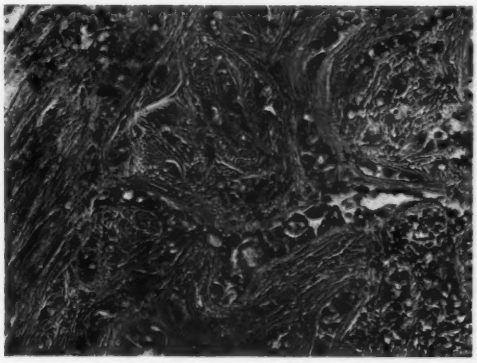

Fig. 4 . Mesothelioma of the epididymis showing a plexiform pattern with strands of epithelium-like cells, smooth muscle and lymphoid nodules (hematoxylin and eosin, ×130).

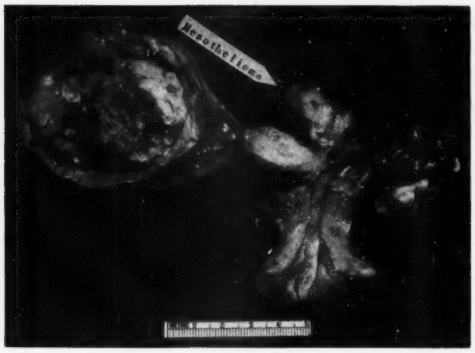

Fig. 5. Mesothelioma of the uterus, showing the solid, trabeculated surface and slight bulging on cut section. Also depicted is a dermoid cyst of the right ovary which was associated with it.

lar to those described previously. Worthy of note was the negative result in 1 case of glycogen stain on fresh tissue fixed in absolute alcohol.

Prognosis. The postoperative course was uneventful in all but 1 case. Thrombophlebitis developed but the patient responded to conservative treatment. Subsequent history was available for 9 of the patients; the interval of time varied from 5 months to more than 5 years after operation. In 6 cases 18 months or more elapsed. In no instance was there any evidence of recurrence or metastasis.

Uterine fibromyomas and peritoneum. Among the 437 tumors of the uterus which resembled fibromyomas in 100 current cases at the clinic in which hysterectomy or myomectomy was performed, 1 case of mesothelioma occurred. Considering only the 228 subserous tumors studied, the incidence of mesothelioma among these tumors was 0.44 per cent. In the 1 case mentioned, diagnosis of mesothelioma was made on gross examination before confirmation microscopically. Though each of the other tumors was checked by microscopic study, in no instance was it felt after gross examination that the tumor was a mesothelioma. All types of degeneration were seen in this study of uterine fibromyomas but caused no problem in differential diagnosis.

In the study of the peritoneum covering subserosal uterine fibromyomas and peritoneum from the posterior surface of uteri, no microscopic findings pertinent to the histogenesis of mesotheliomas were discovered.

MESOTHELIOMA OF THE FALLOPIAN TUBES

The significant details in the 2 cases of mesothelioma of the fallopian tube are as follows:

CASE 1. A married white woman, 51 years old, with 3 children, registered at the clinic on April 3, 1917, with complaints of a "bearing down" sensation and irregular menses. Examination revealed an enlarged uterus. A preoperative diagnosis of probable uterine fibromyomas, with possible intrauterine malignancy, was made. Subtotal abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus weighed 240 grams and showed evidence of metritis, thickened walls, and glandular hyperplasia, but no fibromyomas. The right tube measured 8 centimeters in length; the lumen was patent. On the posterior aspect of this tubal wall was a firm, discrete, ovoid tumor 1 by 0.6 centimeter in diameter. On cut section the tumor was solid, gray, and smooth. Microscopic study revealed a typical mesothelioma with a predominantly tubular pattern. No capsule was present. Most of the numerous glandlike spaces were in a fibrous stroma between internal and external layers of smooth muscle of the wall of the tube (Fig. 9). In one area spaces extended through the outer muscle almost to the serosa. The tumor cells had not invaded the muscle which separated them from the lumen of the tube.

The patient's postoperative course was uneventful. On return for a check-up in 1924, 7 years after operation, there was no evidence of neoplastic recurrence or metastasis. The patient died in 1932 of unknown cause.

Fig. 6. Mesothelioma of the uterus which depicts the subserosal peripheral zone of mesotheliomatous tissue overlying the smooth muscle comprising the rest of the tumor. The glandlike spaces lie in a partially hyalinized fibrous stroma (hematoxylin and eosin, ×27).

CASE 2. A married white woman, 52 years of age, with 9 children, registered at the clinic on January 13, 1950, with a complaint of pain in the left lower portion of the abdomen of 1 week's duration. On examination a large, tender mass was found in the left side of the pelvis, and a polyp in the cervix. The temperature was 101.4 degrees F., and the sedimentation rate was 113 millimeters the first hour (Westergren method). The preoperative diagnosis was infarction of a pelvic tumor. Total abdominal hysterectomy, left salpingo-oophorectomy, appendectomy, and repair of diastasis recti abdominis were performed. The uterus contained on the left an intramural fibromyoma 10 centimeters in diameter with "red degeneration," and a 1 centimeter endometrial polyp. In the midportion of the left fallopian tube was a discrete, subserosal tumor 1 centimeter in diameter, which was found on cut section to be solid and smooth. Microscopically, the tubular pattern of mesothelioma predominated. The tumor was superficial to the tubal muscle separating it from the patent lumen. No continuity of the cells of the tumor with those of the peritoneum was seen. The immediate postoperative course was uneventful.

MESOTHELIOMA OF THE OVARY

Details of the single case of mesothelioma of the ovary in our series follow:

CASE 3. A negro woman, 39 years of age, who was married but had no children, registered at the clinic on August 21, 1922. For 4 years the patient had known of the presence of a growth in the lower portion of her abdomen, associated with inconstant pain and irregular menses. On examination, a large pelvic mass was found; the preoperative diagnosis was uterine fibromyoma. Subtotal abdominal hysterectomy, bilateral salpingectomy and right oophorectomy were performed. The uterus weighed 1,150 grams and contained multiple fibromyomas which measured 0.5 to 10 centimeters in diameter. A right hydrosalpinx was present. The right ovary contained a simple cyst 4 centimeters in diameter. On the anteromedial aspect of the ovary a firm, discrete tumor which measured 1.4 by 1 centimeter bulged both externally and into the cavity of the cyst. On cut section the tumor was grayish yellow, solid and smooth. A typical mesothelioma was found on microscopic study, with a tubular pattern predominating (Fig. 10). The neoplasm was circumscribed but not encapsulated. A thin layer of ovarian tissue separated the tumor from the peritoneum. Smooth muscle was not present. The patient's postoperative course was uneventful; subsequent history could not be obtained.

Fig. 7. Typical microscopic view of a mesothelioma of the uterus which shows the spaces in a fibrous stroma scattered between the smooth muscle (hematoxylin and eosin, ×70).

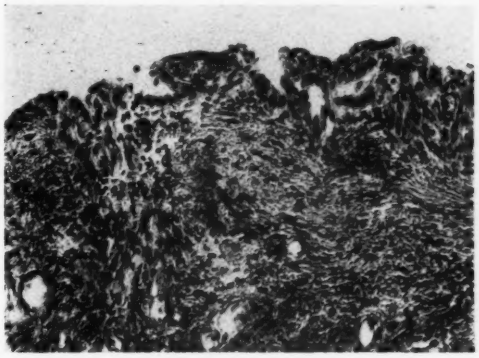

Fig. 8. Mesothelioma of the uterus; note the direct relationship of the glandlike spaces with the serous membrane (hematoxylin and eosin, ×135).

COMMENT

There are 3 possible sources of the neoplasms which we have discussed; namely, (1) epithelium, probably of vestigial mesonephrogenic structures, (2) endothelium of lymphatic channels, and (3) mesothelium of peritoneum and tunica vaginalis. According to embryology as given by Arey, derivation from each of the 3 sources is possible.

The various conclusions in the literature have rested chiefly on interpretation of microscopic findings. While we agree with Bremer and Weatherford that the term "epithelium" should be used for the epidermis and lining of the internal passages, "endothelium" for the lining of the heart and vascular channels and "mesothelium" restricted to the lining of the body cavity and its subdivisions, it is by no means easy to differentiate between these structures in a neoplastic process.

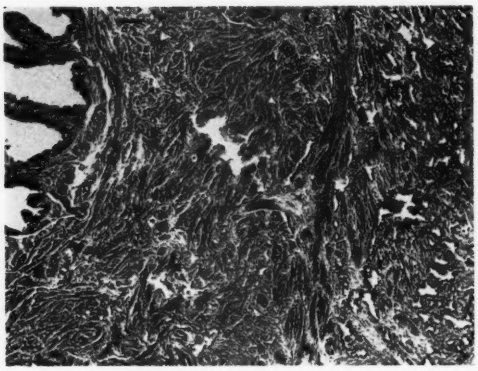

Fig. 9. Mesothelioma of the fallopian tube. Note the cells of the tumor peripheral to the internal layer of muscle from the tubal wall (hematoxylin and eosin, ×30).

Three patterns occur: (1) canalicular, (2) tubular, and (3) plexiform. Proponents of the theory that the tumors are epithelial point out that the groups of cells in the plexiform type and the glandlike spaces in the tubular type resemble other formations of epithelial cells, even adenocarcinoma, and that the flattened cells lining the spaces in the canalicular type have been compressed by the substance within the space. The epithelium-like cells do not resemble epithelium which lines the epididymis and the fallopian tubes, nor any structures normally seen in the uterus and ovaries. Thus, it has been postulated that this epithelium arises from vestigial mesonephrogenic structures. Such structures occur in the broad ligament and near both poles of the epididymis, but relationship of these tumors to such structures has not been demonstrated. Epithelium-like formations do not offer conclusive evidence in favor of an epithelial origin. Such formations also arise from both endothelium and mesothelium, as Ewing and other authors have pointed out, both in neoplastic and inflammatory conditions. It is impossible to settle the question of histogenesis on the basis of the type of cell seen microscopically.

No definite basement membrane is present around the spaces in these neoplasms, which is also true of mesotheliomas and lymphangiomas. Although in most epithelium a distinct basement membrane is found, Maximow and Bloom stated that in the thyroid gland and excretory passages of the urinary system it is absent. Epithelial origin, thus, cannot be excluded on this basis.

Intracytoplasmic vacuoles are a distinctive finding. Signet-ring formation is usually described as being an epithelial characteristic, but vacuolated cells are found in some lymphangiomas and in an occasional case of peritoneal mesothelioma. Coalescence of vacuolated cells to form spaces was described by Morehead who stated that there is a possibility that the sequence of events in the formation of a neoplasm of this type is similar to that in the formation of vascular channels and lymphoid cells in the embryo. However, this method of forming lumens is not restricted to vascular channels.

Scattered infiltration of lymphoid cells and nodular collections of these mononucleated cells, as noted in the stroma of these tumors, may be seen in a variety of neoplasms and are not diagnostic.

Smooth muscle was present in all but 1 mesothelioma. Such muscle is found normally in the epididymis, uterus, and fallopian tubes. It is significant that the tumor in our series in which smooth muscle was not found was the tumor which occurred in the ovary, an organ which normally does not contain muscle. Authors have disagreed on whether the muscle in these tumors showed proliferation or whether it represented inclusion from the surrounding structure. In most of our cases of tumors of the male genital tract, a small amount of muscle was present at the periphery only; this is evidence of inclusion. In 3 instances, however, much more muscle was present than normally would be found in that location and it was found throughout the tumor. This would indicate that in some tumors of the male genital tract proliferation of the muscle had occurred. In the 2 cases in our series of tumors in the fallopian tube, proliferation of muscle was not evident. In the uterus the tumors were comprised to a large extent of smooth muscle with neoplastic cells typically scattered between the bundles of muscle. In the uterus it was concluded that the muscle had undergone active proliferation.

We consider the microscopic findings in our 35 cases most consistent with the diagnosis of

mesothelioma. It is conceded that a diagnosis on this basis is not conclusive. Evans (14) was the only author to describe communication of cells lining the spaces with the peritoneum. In 3 cases of our series areas were noted in which there appeared to be continuity of the cells lining the spaces with those of the serosa, and in another case the cells of the peritoneum resembled those of the spaces beneath. In these 4 cases, the tumors occurred in the uterus, as was true in Evans' case. These cases represent a small percentage of the cases of mesotheliomas which were studied. However, we agree with Evans that the occurrence of all these tumors in proximity to the peritoneum and tunica vaginalis is significant. This evidence strengthens the opinion that these neoplasms have a mesothelial origin.

The most practical feature disclosed by review of the literature and our study is the benign character of mesotheliomas of the genital tract. Despite microscopic features, which at times may be interpreted as malignant, these neoplasms are clinically benign. This is in contrast to mesotheliomas which arise from the peritoneum elsewhere and from the pleura and pericardium. Evans speculated that the direct relationship of these tumors to the generative organs suggested that the histogenic factors concerned may be related to the potentialities of the specialized mesothelium of the urogenital ridge. If this postulate were carried further, perhaps it would lead to an explanation of the unique benign character of these mesotheliomas.

The majority of all extratesticular intrascrotal lesions are inflammatory; nonspecific lesions and those of tuberculous epididymitis are most frequently encountered. The usual occurrence of mesotheliomas of the male genital tract at the lower pole of the epididymis causes confusion with tuberculous epididymitis, which may be localized to this site. Lack of evidence of tuberculosis elsewhere, particularly in the seminal vesicles and vas deferens, is helpful in differentiation. If a hydrocele occurs in association with the lesion an inflammatory or malignant process is considered a possibility. When the lesion is firm, smooth, discrete and appears to be localized to the lower pole of the epididymis, a benign neoplasm should be suspected. Since mesothelioma is one of the most frequent tumors at this site, the possibility of this diagnosis should be entertained.

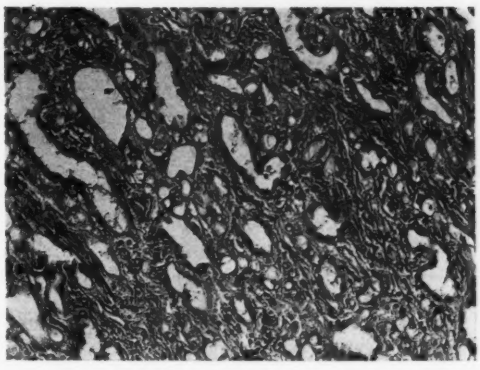

Fig. 10. Mesothelioma of the ovary, showing both glandlike and vascular-like spaces in fibrous stroma (hematoxylin and eosin, ×120).

Treatment should always be excision. When a circumscribed lesion is encountered, simple excision should be performed. After the pathologic diagnosis of mesothelioma is made, further surgical procedure is not necessary. Roentgen therapy postoperatively is not indicated.

Mesotheliomas of the uterus, fallopian tubes, and ovaries are rare and are found incidentally at laparotomy for some associated pelvic condition. In no way are symptoms and physical findings suggestive of the diagnosis. Treatment is usually that demanded by the associated pelvic condition. At operation a small, subserous tumor on the posterior surface of the uterus suggests the possibility of mesothelioma. If the tumor bulges only slightly on cut section, is moist, and is somewhat yellower than the usual fibromyoma, a presumptive diagnosis of mesothelioma can be made. When it is desirous to preserve the uterus and when hysterectomy is not indicated because of other conditions, these benign tumors should be treated by simple excision, as in 2 instances in our series. Mesothelioma of the fallopian tube almost always is associated with fibromyomas of the uterus; 1 of the 2 cases in our series, however, is an exception.

SUMMARY AND CONCLUSIONS

Mesothelioma of the genital tract is a rare tumor which occurs in the epididymis, spermatic cord, and testicular tunics in the male, and in the uterus, fallopian tube, and ovary in the female.

Thirty-five cases of mesothelioma of the genital tract were studied. Eighteen of these neoplasms occurred in the epididymis, 1 in the tunica albuginea, 1 in the tunica vaginalis, 12 in the uterus, 2 in the fallopian tube, and 1 in the ovary.

Three types of patterns are found: (1) canalicular, with large, "vascular" spaces lined by flattened cells; (2) tubular, having glandlike spaces with epithelium-like cuboidal or low-columnar lining cells; and (3) plexiform, with solid strands and nests of epithelioid cells. No true basement membrane is present. Only desquamated lining cells and an occasional mononucleated cell are found in the spaces. Intracytoplasmic vacuoles are a distinctive finding. Fusion of these vacuolated cells seeming to form spaces is seen. Cilia and mitotic figures are not encountered. A weak reaction of material in the vacuoles and in the spaces to mucicarmine is inconstantly noted. In the fibrous tissue stroma lymphoid cells are found, both scattered and in nodules. Smooth muscle in varying quantities occurs in tumors in all locations except the ovary; in some cases proliferation of the muscle has occurred. Reticular fibers form a network between the spaces, and fibers of elastic tissue are infrequent.

Evidence regarding the histogenesis of these unique neoplasms remains inconclusive. Certain microscopic features favor each of the possible sources of origin; that is epithelium, endothelium, and mesothelium. We consider the microscopic findings in our study as most consistent with a diagnosis of mesothelioma. The location of all the tumors in the genital tract in proximity to mesothelium of peritoneum or tunica vaginalis is considered significant. Demonstration of apparent communication of lining cells of the neoplastic spaces with cells of the overlying serosa in 3 cases of mesothelioma of the uterus is further evidence in favor of mesothelial origin.

Though microscopic features at times may suggest malignant disease, mesotheliomas are clinically benign. Treatment of mesothelioma should consist of excision of the tumor. The duration before operation, when known, is usually long and growth is slow. With few exceptions, the tumor has been found to be well circumscribed. Metastasis at the time of operation has not been found. Subsequent history, as long as 30 years after operation in 1 case in our series, has never revealed local recurrence or metastasis.

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CARCINOMA OF THE BUCCAL MUCOSA: TREATMENT AND END RESULTS

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CARCINOMA of the inner surface of the cheek is a disease that can be readily visualized and for which radical treatment gives a high percentage of good results. The co-operation between the family physician and the surgeon, so that these patients receive the most efficient early treatment, will always tend to produce the best possible results.

The majority of carcinomas of the buccal mucosa are squamous cell epitheliomas. Jorstad, in a study of 1,561 patients with carcinoma of the oral cavity, found that all but 10 had lesions of the squamous cell type. Archer and Morris reported that 98 per cent of the tumors in their series of 203 cases of intraoral carcinoma were squamous cell carcinomas. Martin and Pflueger reported, in their study, that 95 per cent of 99 patients with carcinoma of the cheek had squamous cell carcinoma.

PRESENT STUDY

This study of carcinoma of the buccal surface of the cheek covers 107 consecutive cases encountered at the Mayo Clinic in the decade January 1, 1932, through December 31, 1941. This period was chosen to allow a minimal 5 year follow-up in all cases. Follow-up was carried out by examination at the clinic or by sending statistical letters containing pertinent questions regarding recurrence, metastasis, further treatment, and medical care for the original lesion, or by both methods. Ninety-three patients, or 87 per cent, were traced 5 years or more.

The criteria of eligibility of each case were (1) histopathologic proof of the disease and (2) primary origin within the anatomic confines of the cheek to as accurate a degree as could be determined from the physical examination, the history obtained from the patient or the correspondence with the referring physician.

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Abridgment of a thesis submitted by Dr. Jackson to the faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Plastic Surgery.

INCIDENCE

Lawrence and Brezina stated that cancer of the oral and pharyngeal mucous membranes constitutes 3 per cent of all cancers and causes approximately 3,700 deaths yearly in the United States registration area.

In Archer and Morris' group of 203 patients with intraoral carcinoma, 18 or 8.8 per cent had their lesions on the buccal mucosa, 85 per cent were males and the average age compared favorably with that given by other authors (60 to 65 years).

Beiswanger and Stenstrom reported 49 cases of carcinoma of the cheek, with an average age of 65 years, the majority of patients being between 50 and 79 years.

Burford and Ackerman stated that carcinoma of the buccal mucosa accounts for 10 per cent of all intraoral neoplasms, that 90 per cent of such carcinomas occur in males, and that the disease is primarily one of old age.

Figi gave the ratio of males to females as 8:1 to 10:1, with the most frequent incidence being in patients more than 40 years of age.

Jorstad reported 70 cases of carcinoma of the cheek. The average age was 64.5 years. The youngest age was 35 years, the oldest 83.

Lawrence and Brezina reported 13 cases of primary carcinoma of the buccal mucosa and 1 case of secondary carcinoma. Nine patients were males and 5 were females.

Liljencrantz, in a survey of 1,000 cases of oral carcinoma, reported an incidence of 10 per cent in the buccal mucosa.

Martin and Pflueger reported 99 cases of carcinoma of the cheek and stated that it constitutes 9.5 per cent of all intraoral tumors.

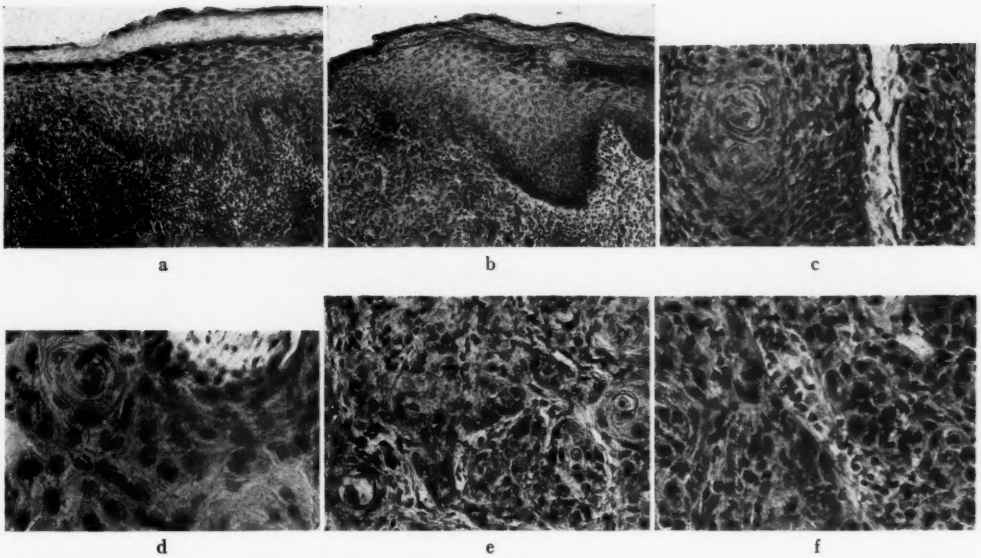


Fig. 1. Sections stained with hematoxylin and eosin. a, Leucoplacia and epithelial hyperplasia (×80). b, Transition from leucoplacia and epithelial hyperplasia to squamous cell epithelioma, grade 3 (×65). c, Squamous cell epithelioma, grade 1 (×140). d, Squamous cell epithelioma, grade 2 (×170). e, Squamous cell epithelioma, grade 3 ×140). f, this section shows squamous cell epithelioma grade 4 (×175).

The average age was 59 years and the ratio of males to females was 9:1.

In our series of 107 cases, the average age was 62 years, with a sex ratio of 102 males to 5 females, or about 20:1. Eighty-five per cent of the lesions occurred in patients between the ages of 50 and 79 years. The youngest patient was 31 years of age, the oldest 87 years.

ETIOLOGY

Ewing stated that buccal and lingual cancers are almost always due to one or more of the following factors: syphilis, tobacco, and decayed teeth. The majority of other authors have felt that chronic irritation is an important etiologic agent and have added to the abovementioned three factors a number of others, such as broken or sharp teeth, ill-fitting dental appliances, chronic infections of the mouth, malhygiene, and objects (pins, nails, sulfur) held in the mouth in certain occupations (1, 3, 5, 9, 15, 21, 22). We have encountered a few cases in which it appeared that jagged teeth or ill-fitting dentures may have been the chief etiologic agent, but in general we do not feel that such factors occur sufficiently often to warrant so much emphasis.

Archer and Morris in a study of 203 cases of oral carcinoma stated that trauma and irritation from broken teeth and artificial dentures did not appear significant as etiologic agents and that the relationship of syphilis appeared significant only in carcinoma of the anterior part of the tongue.

LEUCOPLACIA

It is generally agreed that leucoplacia is a frequent precancerous lesion (1–3, 5, 9, 14, 15, 17, 21, 22, 29).

The incidence of leucoplacia as given in the literature varies from 10 per cent (17) to 70 per cent (21). In our series of cases 15 per cent of the carcinomas were associated with leucoplacia. All such lesions were grade 1 or grade 2 squamous cell carcinomas. Figure 1a demonstrates the appearance of the lesion in a case of leucoplacia. Figure 1b shows the transition from leucoplacia and epithelial hyperplasia to a grade 3 squamous cell epi-

Fig. 2. Gross appearance of a squamous cell epithelioma of the buccal mucosa.

thelioma. The appearance of lesions of different grades is illustrated in Figure 1c to f.

DIAGNOSIS

Often the gross appearance of a carcinoma of the cheek is sufficiently typical to permit a clinical diagnosis (Fig. 2). The lesion may have a warty, papillary appearance, or it may be a fissure or ulceration with elevated, firm margins and subjacent induration.

Any ulceration of the inner part of the cheek that persists after 2 or 3 weeks should be subjected to biopsy and a frozen section should be made for microscopic diagnosis. The biopsy is preferably done by the physician who will carry out the regimen of treatment. Otherwise the inflammatory reaction which ensues may obscure the limits of the lesion by the time the patient is operated on.

All of the lesions in our series were graded 1 to 4 on the basis of Broders' (8) histopathologic criteria; 72 per cent were graded 1 or 2 (Table I and Fig. 1c, d, e and f).

TABLE I.—INCIDENCE ACCORDING TO GRADE OF MALIGNANCY

Malignancy, grade	Cases	
	Number	Per cent
1	37	34.6
2	40	37.4
3	23	21.5
4	7	6.5
Total	107	100.0

TREATMENT

The treatment of choice in carcinoma of the inner part of the cheek should be complete destruction of the primary lesion with surgical diathermy and dissection of the submental, bilateral submaxillary and upper deep cervical lymph nodes, followed by a block dissection if a node with a metastatic lesion is found. Irradiation therapy should be used in addition to surgical treatment when there is involvement of the nodes.

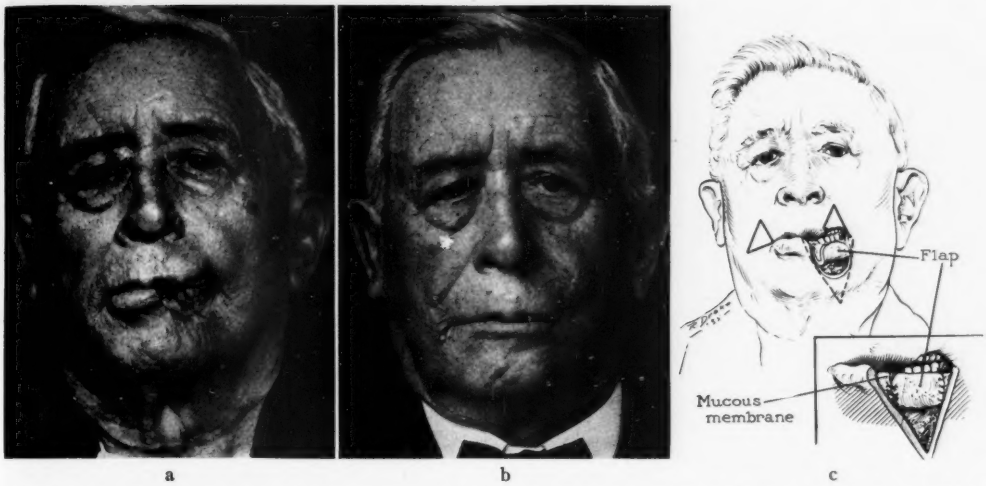
In the presence of a high degree of histopathologic activity, marked extent of the primary lesion, previous insufficient treatment, extensive involvement of the lymph nodes or a combination of these factors, irradiation may be all that will help.

Thus, lesions of grade 1 and grade 2 (7, 8), unless recurrent or extensive, are removed surgically. Grade 3 and grade 4 lesions receive both thorough surgical treatment and supplementary irradiation. It is imperative that the treatment be sufficiently radical to effect complete destruction of the lesion. If the upper or lower jaw is involved, the surgical diathermy will produce a sequestrum which must be removed in 2 months. If the epithelioma infiltrates the overlying skin, a perforation is unavoidable. Plastic correction may be carried out after the lapse of a year to be fairly sure that there will be no recurrence.

It is equally important that the initial plan of treatment include the cervical lymphatics. Grade 1 lesions, unless very extensive or recurrent, do not require a prophylactic dissec-

TABLE II.—FIVE YEAR SURVIVALS

	Traced patients		
	Total	Living after 5 years	
		Number	Per cent
Patients with microscopically proved metastasis	24	5	20.8
Patients with clinical metastasis (treated by irradiation)	10	0	0
Patients without metastasis	59	43	72.9
Total	93	48	51.6



a b c

Fig. 3. a, Appearance prior to reconstruction. b, A flap was turned in for a lining, one edge being sutured to the mucous membrane of the lip and the other to the mucous membrane of the cheek. Then by removing the triangles of tissue from the upper lip and cheek at each angle of the mouth, the skin edges of the defect, which were cut in the form of a "v" and which were deeply undermined, could be brought together over the flap to close the defect. (This illustration is reproduced from New, G. B., and Figi, F. A., 26); c, Postoperative appearance.

tion of the lymph nodes because of their low incidence of metastasis. In grade 2 and grade 3 lesions, the treatment of choice is a prophylactic dissection of the submental, bilateral submaxillary, and upper deep cervical nodes. The lymph nodes are examined microscopically by the frozen section technique. If metastatic lesions are present, the operation is continued as a block dissection on the involved side, the sternocleidomastoid muscle, the internal jugular vein and usually the spinal accessory nerve being sacrificed. In grade 4 lesions, dissection of the lymph nodes is done and this is followed by irradiation, if the extent of the local lesion, the previous treatment, and the status of the cervical nodes warrant it.

Contraindications to dissection of the lymph nodes include advanced age, poor general physical condition, fixation of metastatic masses, and bilateral metastasis. If a metastatic lesion in a submaxillary node involves the lower jaw, the bone is cauterized at the time of the dissection.

END RESULTS

Twenty-four of the 93 traced patients, or 25.8 per cent, had microscopically proved

TABLE III.—TREATMENT, METASTASIS, AND SURVIVAL AS RECORDED IN THE LITERATURE

Author and treatment	Patients			
	Total	With metastasis at sometime during disease		Living after 5 years, per cent
		No.	Per cent	
Beiswanger and Stenstrom Irradiation, primary lesion; irradiation and operation, metastatic lesions	49	32	65.3	18
Berven Irradiation and operation for primary and metastatic lesions	81			26
Duffy Irradiation, primary lesion; irradiation and operation, metastatic lesions	74	15	20.3	
Jorstad Operation for primary and metastatic lesions	70	27	38.6	
Richards Irradiation, primary lesion; operation, metastatic lesions	55	24	43.6	12.7
Martin and Pflueger Irradiation, primary lesion; operation (1935) and irradiation, metastatic lesions	99	56	56.6	30
Mayo Clinic Operation for primary and metastatic lesions; supplemental irradiation	107 (93 traced)	24	25.8	51.6

metastatic lesions, which were confined to the same side in all but 1 case.

Fifty-nine patients had no evidence of metastasis (Table II). Dissection of the lymph nodes was performed on 30 of these. The remaining 29 patients had grade 1 lesions and did not have such dissections. Forty-three of the 59 patients, or 72.9 per cent, survived 5 years (Tables II and III). Twenty-four patients had microscopically proved metastasis; 5, or 20.8 per cent, survived 5 years. Ten patients had only clinical evidence of metastasis and received irradiation therapy to the neck; there were no 5 year survivors. Forty-eight of the 93 traced patients, or 51.6 per cent, survived 5 years. A comparison between these results and those reported in the literature is given in Table III.

The grade of the primary lesion materially influenced the survival rate (Table IV). In general, the 5 year survival rate decreased as the grade of malignancy increased.

RECONSTRUCTION OF DEFECTS OF THE CHEEK

Two major sequelae to the eradication of carcinoma of the buccal mucosa may require reconstructive or restorative surgical treatment. These are perforation of the cheek and intraoral scarring of such an extent as to encroach on function. Occasionally, a perforation into the antrum may result from destruction of a primary lesion involving the cheek and upper jaw.

It is preferable (26) to delay reconstruction for several months, in order that possible recurrence may be detected early, should it occur. If recurrence takes place under a reconstructed area, it is extremely difficult to detect it early, and by the time it is recognized, destruction of the transplanted tissues as well as much adjacent tissue may be required (26). The recurrent growth may reach the stage of inoperability before it is recognized clinically. In general, one or more of the following factors warrants a longer delay before repair is undertaken: extensive lesions, previously irradiated lesions, lesions of high histopathologic activity, and lesions which secondarily involve bone (26).

TABLE IV.—GRADE OF MALIGNANCY AND FIVE YEAR SURVIVAL

Malignancy, grade	Traced patients		
	Total	Living after 5 years	
		Number	Per cent
1	30	25	83.3
2	35	16	45.7
3	23	5	21.7
4	5	2	40.0
Total	93	48	51.6

According to MacFee, Gussenbauer, in 1877, appears to have initiated the idea of replacing mucous membrane with skin in repairing defects of the cheek. He used a quadrilateral open flap, the pedicle of which was in front of the ear. This was turned in for a lining and later a similar adjacent flap was used to provide external skin covering.

ADJACENT TISSUE

Good blood supply and elasticity are essential to insure the use of adjacent tissue (24). Utilization of adjacent tissue is the procedure of choice, provided the deformity is not increased and a good functional and cosmetic result is obtained (24). Furthermore, the final result is achieved with a considerable saving of time (24).

A hinged flap may be used to be turned into the defect to serve as a lining (26). However, it must be elevated and delayed to insure adequate circulation before being turned in (26). The resulting raw surface may be covered by a rotational advancement flap (22, 27), or, if this surface is too large, by a thick split, or full-thickness, graft (26).

Figure 3 illustrates the use of adjacent tissue.

DISTANT TISSUE

If the defect is too large, or if dense scarring, poor vascularity, or proximity to an orifice preclude the use of adjacent tissues, then tissue brought in from a distance must be used (24).

Figure 4a shows the various types of pedicle flaps, open and tubed, which may be useful in the management of the larger perforations of the cheeks. The more practical ones are the forehead open flap and the acromioclavicular flap (25).

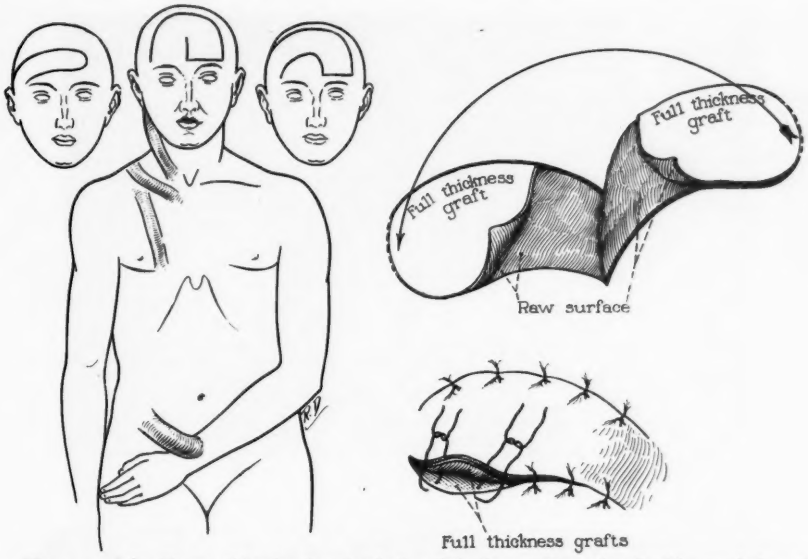


Fig. 4. a, left. Types of forehead and tubed pedicle flaps. (Reproduced with permission of New and Erich, 25; and Am. J. Surg.). b, Method of lining a forehead or sickle flap.

FOREHEAD FLAPS

These are horseshoe-shaped flaps which incorporate in their pedicles either the supraorbital or temporal vessels. They have the advantages of furnishing skin of an excellent texture and color index and of requiring a considerably shorter length of time before being ready for use than pedicled skin from elsewhere (24). However, their use produces additional visible scarring (24). This may be undesirable in a man, although a woman can frequently arrange the hair to conceal most of the scarring.

It has been largely to offset these disadvantages that one of us (New) has for several years used the sickle flap. This is a combination scalp and forehead open flap, having incorporated in its pedicle branches of the superficial temporal artery. The tissue actually used in closing the cheek defect is the bay of skin lateral to the midline and just below the hairline of the forehead (24). The sickle flap finds its greatest usefulness in partial reconstruction of the nose. It can, however, be used in defects of the anterior superior part of the cheek. Figure 4b shows the procedure for lining the distal end of a forehead or sickle flap. This lining is supplied by a free skin graft, either a thick split, or full-thickness graft, usually applied both to the undersurface of the distal part of the flap and to the distal part of the bed from which the flap was made. These grafts are applied at the time of the initial elevation of the forehead or sickle flap, the flap being left attached proximally and distally.

TUBED FLAPS

The acromioclavicular tubed flap may be used in several ways to repair defects of the cheek after the lapse of sufficient time and partial severing have insured adequate circulation (6 to 8 weeks). Its distal end may be lined with a split or full-thickness skin graft, or lined by doubling under the distal portion on itself (25). A week or 10 days later the distal end may be swung into the defect of the cheek after the scarring has been excised, suturing skin graft lining to mucous membrane and skin surface to adjacent skin of the cheek. After 2½ to 3 weeks the tube is partially cut across and a week later completely severed. At this time the remainder of the periphery of the defect of the cheek is pre-

Fig. 5. a, Preoperative appearance. b, Postoperative appearance. c, Closure of a defect at the angle of the mouth by means of a tubed skin flap. In the procedure illustrated, the tube is used both for lining and for covering of the reconstructed region. The tube is first sutured around the defect with its skin surface directed oralward. The tube is then folded on itself and, when sutured around the defect, forms the external surface for the reconstructed part. The excess fat is removed later. In this particular case the residual scarring inside the left cheek secondary to removal of an epithelioma produced complete ankylosis. After excision of this scar tissue, the tubed flap was inserted within the mouth, as is shown, to cover the raw area and correct the ankylosis. (This illustration is reproduced from New, G. B. and Figi, F. A., 26).

pared, and the edges of the transferred tissue are sutured into position. The balance of the tube may be discarded or replaced into the area from which it was originally constructed.

The distal end of the acromioclavicular tube may be transferred unlined into the defect, so as to replace lost mucous membrane (25). A rotational advancement flap may then be turned into the defect to provide external skin covering (Fig. 5).

Figure 6 illustrates the use of distant tissue where bulk, as well as covering and lining, was necessary.

The sternal end of an acromioclavicular tubed flap furnishes skin of a better color index than other tubed flaps about the trunk or

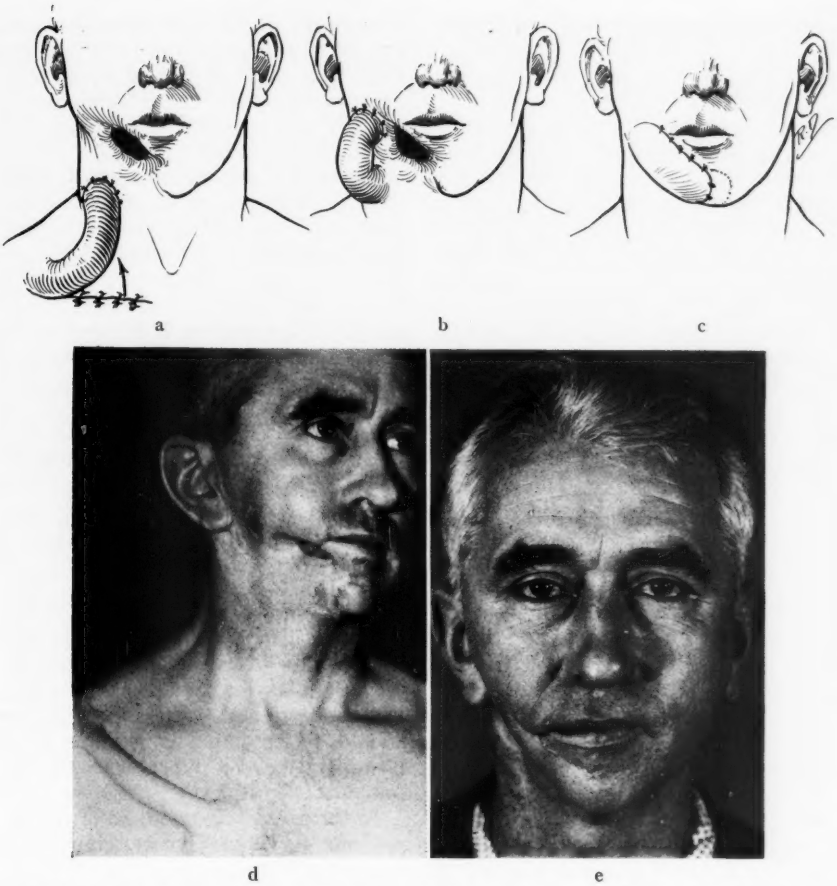


Fig. 6. Closure of a large defect of the cheek and lower lip below the vermilion border by means of a clavicular tube flap. a, The mesial end is transferred to the right midcervical region. b, The lateral end is elevated and sutured to the posterior margin of the defect. c, The mesial end is removed from the cervical region and attached to the mesial margin of the defect. Some of the fat in the tube is tucked under the mesial margin (indicated by the dotted line) in order to give the proper fullness to the chin. Later the superior and inferior surfaces of the tube are incised and sutured to the corresponding margins of the defect. Since none of the fat in the tube is removed, a well rounded contour is obtained in the reconstructed region. (Reproduced with permission of New and Erich, 25). d, Preoperative appearance. e, Postoperative appearance.

arm, but inferior to that furnished by a forehead flap (24). The acromioclavicular flap, as well as the other tubed flaps, requires considerably more time. The main advantage is that the scarring of the donor area can be covered by wearing apparel, particularly on a man.

The thoracoepigastric tubed flap (30) is the only other one derived from the trunk which is long enough to reach from its site of construction to the defect. Most of the shorter chest and subaxillary tubes must be moved up by the caterpillar or waltzing method, or else carried up to the cheek by using the forearm or wrist as an intermediate source of blood supply (25). These require, in general, an even longer time to reach their destination than do the acromioclavicular tubed flaps and

are poor matches as regards texture and color index (25).

INTRAORAL SCARRING

The destruction of carcinoma of the cheek by electrocoagulation is followed promptly by granulation, after separation of the slough. The degree of limitation of motion varies greatly, depending on the extent and situation of the scarring (26). At times there may be complete ankylosis, and restoration of lost lining is necessary for correction. This is accomplished by freeing the scarred attachment to the mandible and relining this portion of the mouth with a stented split skin graft (26).

Erich has used successfully a device known as a bite-opener, which is a modification of an apparatus originally introduced by Blair and Ivy. Erich's modification consists of two thin horseshoe-shaped metal plates approximately the size and configuration of the dental arches, attached at right angles to counteracting metal arms in such a way that rubber bands hooked over the ends of these arms exert a separating force on the two metal plates. Thus, the two plates are introduced closely approximated between the teeth, and there results a bite-opening action. The patient uses this apparatus 30 minutes, twice daily for 6 months. By the end of this time an appreciable improvement in the amount of separation of the upper and lower incisor teeth will usually have occurred, due to gradual stretching of the scarring in the posterior commissure between the upper and lower jaws.

The scarring may be so dense that the ankylosis can better be corrected by an osteotomy through the horizontal ramus of the mandible anterior to the scarring. A false joint is thereby created.

Scarring may obliterate the buccoalveolar sulcus and make it impossible for the patient to wear a denture. This may be corrected by a modification of the Esser epithelial inlay. An occlusal cap metal splint is constructed and cemented on the teeth in the region of the obliterated sulcus. The scarring is dissected out and a pocket created which restores the continuity of the sulcus. Dental impression compound is molded around a light metal framework which is, in turn, designed to be fastened to the cap splint by small screws. A split skin graft is lightly cemented to the dental compound stent, which is inserted into the raw pocket, and screwed in place. A moderate pressure dressing is applied to immobilize the overlying soft tissues and left for 10 to 14 days. Then an acrylic stent or denture is made and the patient instructed to remove the stent only a few minutes at a time for cleaning purposes. Otherwise the pocket may contract enough to prevent replacement of the stent. If the patient is edentulous, a flange extension of dental compound is applied to the denture and covered with a skin graft. Later a flanged denture is built.

Perforation into the antrum is corrected by means of a denture with an obturator designed to occlude the perforation. If the perforation is small enough, surgical closure may be performed after a delay of six to nine months.

CONCLUSIONS

The treatment of epithelioma of the cheek should be complete removal of the local lesion followed by dissection of the lymph nodes. A block dissection should be done if metastatic lesions are found. The regional lymphatics should be irradiated in grade 4 lesions and postoperatively if metastatic growths were found at operation.

In the series presented, 48 of the 93 traced patients survived 5 years, giving a survival rate of 51.6 per cent.

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EDITORIALS

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TREATMENT OF HYPERTHYROIDISM

THREE relatively safe and effective means now exist for controlling hyperthyroidism: (1) subtotal thyroidectomy after preparation with propyl thiouracil and iodine, (2) prolonged administration of propyl thiouracil, and (3) radioactive iodine.

Sufficient time has not yet elapsed to allow a final appraisal of the last two methods of treatment, and it will be many years before one can be certain that they will not be followed by delayed complications. Nevertheless the immediate results of treatment with radioactive iodine (I^{131}) are so satisfactory, and the method is so simple and apparently so safe, that its use undoubtedly will be extended unless untoward late results appear.

When an anatomic *thyroidectomy* is performed by a competent surgeon who identifies and preserves the recurrent laryngeal nerve and parathyroid bodies, the incidence of persistent tetany and of permanent paralysis of a laryngeal nerve should be less than 1 per cent. The mortality rate should be only a small fraction of 1 per cent if all patients whose hyperthyroidism is severe or whose general condition is poor are prepared with an antithyroid drug and with iodine until the hyperthyroidism is completely controlled. But despite this low mortality and morbidity following thyroidectomy, both prolonged treatment with propyl thiouracil and treatment with radioactive iodine are associated with less immediate risk than operation.

It is necessary to draw a sharp distinction between Graves' disease and nodular goiter with hyperthyroidism because the results of their treatment are quite different. If a conventional type of nonanatomic, partial thyroidectomy is performed for Graves' disease the incidence of recurrence is between 10 and 20 per cent in the first 5 to 10 years after operation. Following more radical anatomic operations the recurrence rate may be as low as 3 per cent. But after operations for nodular goiter with hyperthyroidism the incidence of recurrent hyperthyroidism is only about 1 per cent, regardless of the type of operation performed.

Hypothyroidism follows subtotal thyroidectomy for Graves' disease in approximately 4 per cent of the patients operated upon in the conventional manner, but occurs in over 20 per cent of those operated upon by the more radical anatomic technique. Yet severe hypothyroidism almost never follows subtotal thyroidectomy for nodular goiter with hyperthyroidism and mild hypothyroidism occurs in only about 3 per cent of the cases regardless of the technique followed. In short, thyroidectomy for Graves' disease is attended by a high incidence, either of recurrence of the hy-

perthyroidism or of postoperative myxedema depending on the amount of thyroid tissue removed, whereas the incidence of these complications following operations for nodular goiter with hyperthyroidism is low regardless of the technique employed. Thyroidectomy is therefore a less satisfactory treatment for Graves' disease than it is for nodular goiter with hyperthyroidism.

Propyl thiouracil, if given in doses of 300 to 400 milligrams spaced throughout the day, is capable of controlling hyperthyroidism in about 95 per cent of the patients with Graves' disease. Unfortunately, only about 50 per cent of the patients treated remain well after withdrawal of therapy and there is no way of predicting in which patient the hyperthyroidism will remain in remission.

In many cases long-standing or permanent remissions can be induced if the hyperthyroidism is controlled completely for a year. But since the recurrence rate is so high it is not wise to promise the patient a medical cure, and it is preferable to point out from the first that more definitive therapy may be required if propyl thiouracil fails. The rate of recurrence is particularly high in those patients who have large goiters and severe hyperthyroidism, who have severe recurrent hyperthyroidism, or who have hyperthyroidism associated with nodular goiters. Since most patients tire of indefinitely prolonged medical treatment and since prolonged remissions are rarely induced in patients who respond poorly or whose hyperthyroidism recurs after withdrawal of therapy, definitive treatment of hyperthyroidism should not be delayed too long.

Radioactive iodine, if given in large enough repeated doses, theoretically should control all hyperthyroidism regardless of whether it is associated with Graves' disease or nodular goiter. The hyperthyroidism of nodular goiter, however, is much more resistant than that of Graves' disease in which it is controlled by a single treatment in 65 per cent of the cases. From two to three times as many treatments and three times as much radioactive iodine are required to control the hyperthyroidism of nodular goiter as that of Graves' disease.

The nodular goiters do not disappear, as the diffuse ones do, but may remain the same size or diminish to one-half or one-third of their original size. Radioactive iodine therefore is not a satisfactory treatment for nodular goiter but merely controls the associated hyperthyroidism.

Hypothyroidism is induced in about 10 per cent of the patients with Graves' disease and in few if any patients with nodular goiter, a situation comparable to that following thyroidectomy.

Hyperthyroidism may recur in the first 2 years after treatment in between 1 and 2 per cent of the patients treated with radioactive iodine. No untoward side effects other than an occasional transitory exacerbation of the hyperthyroidism have been observed in a series of 400 patients treated with radioactive iodine.

It is apparent that thyroidectomy is more effective than either radioactive iodine or propyl thiouracil in the treatment of nodular goiter with hyperthyroidism. But the immediate safety, the economy, and the ease of treatment with radioactive iodine would render it the preferred treatment for all patients with Graves' disease if one could be certain that it would not prove ultimately to be carcinogenic. Because of this possibility it has not been used routinely in patients under 45 years of age. But in older patients, in those with complications which increase the hazards of thyroidectomy, and in those who have recurrent hyperthyroidism, the possibilities of mortality and morbidity should be carefully appraised before operation is undertaken. In selected cases either prolonged treatment with propyl

thiouracil or definitive treatment with radioactive iodine may be safer and just as satisfactory as thyroidectomy. Finally, if thyroidectomy is to be employed as the standard treatment of Graves' disease, it is important that its morbidity and mortality be maintained at a level low enough to justify its use in cases in which other methods of treatment are equally acceptable. GEORGE CRILE, JR.

SHOULD OPERATION BE DISCARDED IN TREATING PERFORATED PEPTIC ULCER?

ACUTE perforation of peptic ulcer produces such dramatic symptoms that both the patient and his family usually realize that a severe intra-abdominal accident has occurred. If the condition is diagnosed correctly, and prompt, energetic, and proper treatment instituted, the mortality rate, which was quite high 15 to 20 years ago, should be relatively low. During the past two decades in this country and in Canada, the usual treatment of acute perforation of peptic ulcer has consisted of operation with simple closure of the perforation as soon as possible after the general condition of the patient warrants operation, provided that the perforation has not been present more than 24 hours. With little or no change in the operation itself, the mortality rate has decreased during these years because of the introduction of accessory aids or better application of already well known principles. Of prime importance have been (1) improvements in anesthesia; (2) better and more widespread use of blood transfusion and other intravenous fluids, both in preparation for operation and during the postoperative period; (3) the use of continuous gastric suction according to the method of Wangensteen; and (4) the routine use of chemotherapeutic and antibiotic agents.

During the past few years, nonoperative methods of treating this condition have been advocated by some surgeons who make use of the principles just mentioned, namely, intravenous alimentation, continuous gastric suction, and antibiotics, without operation. The rationale leading to the adoption of this method was the frequent finding at operation that the perforation had already sealed off by becoming adherent to some neighboring structure, and that in such cases operation added no additional security, and might entail disturbing the sealed off opening and causing potential spreading of infection. In the beginning, this nonoperative treatment was advised only in those cases in which there was escape of a relatively small amount of gastric content, but more recently it has been used by some surgeons in all cases diagnosed as perforated ulcer. The results obtained by this method are said to be excellent, and the mortality low, although insufficient data have been published to determine as yet what the mortality rate is likely to be. Most of the published reports give mortality rates in the neighborhood of 10 per cent although Seely has reported 34 consecutive cases without a death and is said to have a much larger series now, still without a death.

Before deciding to discard the time-honored method of early operation with closure of the perforation, it would seem desirable to review present day experience with this method. A recent report by McElhinney of the results obtained at the Cincinnati General Hospital for the five year period 1945 to 1949 inclusive seems pertinent. There were 128 cases of perforated ulcer seen during this period with eight hospital deaths, an over-all mortality of 6.2 per cent. Six patients were not operated upon, three of whom died. In the 122 patients operated upon there were five deaths, an operative mortality of 4.1 per cent. One of these

deaths occurred on the second postoperative day and was due to rupture of an aortic aneurysm in a patient getting along well otherwise. One death occurred in a patient with far advanced pulmonary tuberculosis and two others in patients with serious cirrhosis of the liver with ascites. It is obvious that in four of the five patients who died, there was associated serious disease which undoubtedly contributed to the fatal outcome. All of the patients in this series had continuous gastric suction instituted as soon as the diagnosis was suspected, all received penicillin, and many received sulfadiazine also. The operative procedure was simple closure of the ulcer in all except three cases, and in these, gastric resection was performed because all three had previously survived an acute perforation and were thought to need more than simple closure. The six patients not operated upon all reached the hospital more than 24 hours after the acute perforation, and previous experience had indicated that operation for closure of the perforation was not advisable in such a group.

This operative mortality is low according to previously accepted standards and is within the same range as that reported by advocates of the nonoperative method. There is also reason to believe that it can be further improved. For instance, in this particular series there was no death in any of the 54 patients operated upon within six hours of the perforation. Other factors need also to be considered in deciding upon the relative value of the two methods. For example, it is extremely difficult to determine, prior to operation, how much soiling of the peritoneal cavity has occurred, and whether the perforation has sealed off or will seal off spontaneously. It is well known by those who have operated upon many of these cases that a patient showing relatively minor symptoms and signs may prove at operation to have a large amount of gastric or upper intestinal content free in the peritoneal cavity while in another with marked signs of peritoneal irritation there may be relatively little soiling. Another fact well established by operation and postmortem examination is that large perforations do not tend to seal off spontaneously, and it is not uncommon to find a large perforation just beyond the pylorus, leaking duodenal contents, even though the stomach is completely empty because of a well functioning gastric suction tube. Still another factor that has to be considered is the possibility of incorrect diagnosis. Those surgeons who are called upon to operate frequently for acute intra-abdominal conditions are well aware that even though their experience be considerable, it is impossible to make a correct preoperative diagnosis every time. Not infrequently one operates with the diagnosis of acute perforated ulcer and finds instead, acute perforation of the appendix, of the gall bladder, or of a diverticulum of the colon, and even at times strangulated or devitalized bowel, conditions which are better treated by operative than by nonoperative methods.

It is of course well recognized that factors other than the method of management affect the mortality rate. For example, it has been repeatedly demonstrated that the time elapsing after perforation and until treatment is instituted is extremely important. The mortality rate increases as this time is prolonged. In the Cincinnati General Hospital series referred to, there was no death in patients seen within six hours of perforation, while in the six patients seen 24 hours or more after perforation, there were three deaths. A second factor is the age of the patients. It has been frequently shown in the past when mortality rates were higher than at present, that there was an almost direct correlation between mortality rates and the ages of the patients, those in the older age group showing consistently higher death

rates. The third important factor is the presence of serious associated illness, the acute perforation being superimposed upon this condition. In many instances the patient may be a chronic invalid, with cirrhosis, hypertension, arteriosclerosis, diabetes, or advanced renal disease and an accident like acute perforation in such individuals is much more serious than it is in a group of young, relatively robust persons. For these reasons, in comparing mortality rates it is important to consider critically these factors.

At the present time it seems desirable to continue with operative treatment of acute perforated ulcer until or unless it can be proved conclusively that the nonoperative method offers lower mortality and as good or better end results than those attained by the operative method. It may eventually be shown that a combination of the two methods will give the lowest mortality. For example, it was common practice 10 to 15 years ago to operate on all patients regardless of the duration of the perforation. It is now clearly recognized by those who advocate operation that to proceed with the idea of closing the perforation has no place in the treatment of patients who have had the perforation for 24 hours or longer. By this time, sealing off has occurred, or else there is widespread soiling with beginning peritonitis. Under such circumstances, operation to seek out and close the perforation probably does more harm than good, although a small incision to drain an abscess or an intra-abdominal collection of fluid may be necessary then or at a later time. Perhaps in the interest of obtaining lower mortality rates, this 24 hour period should be reduced to 20 hours or even to 18 hours and no patient operated upon for closure of an ulcer if perforation has been present for more than 18 hours. The nonoperative method also would seem to be indicated in cases in which there is doubt about the diagnosis and in situations in which a surgeon or satisfactory hospital facilities are not available. The earlier gastric suction is started and antibiotics are given, the lower the mortality will be either with or without operation, so these measures should be instituted promptly as soon as the diagnosis is suspected.

Finally, surgeons need to consider the relative merits of gastric resection in place of simple closure for selected cases of acute perforation. This method has long been advocated on the European continent, but it has never been popular in this country, though a few surgeons, especially Bisgard, have recommended it. Enough experience has now accumulated to show that in the hands of a surgeon competent to carry out a gastric resection quickly and skillfully, this operation can now be performed without undue risk in patients with acute perforation of an ulcer. It would seem to be wise to restrict its use to those cases in which acute perforation is superimposed upon some other complication of ulcer, such as previous perforation, hemorrhage, or obstruction. It should be used only in a patient seen soon after the perforation, whose general condition is good. If these limitations are observed, it may develop that this method is accompanied by as low a mortality rate as is simple closure of the perforation, with better final or long range results.

M. M. ZINNINGER.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE author of *An Atlas of the Blood and Bone Marrow*,[1] who is primarily a pathologist, planned this book in the hope that it would be useful to clinicians, clinical hematologists, pathologists, and medical technologists. This hope cannot fail to be realized.

The first part of the book is devoted to the development and function of the hematopoietic tissues and the normal blood and bone marrow. This is followed by the larger section on disorders of the blood and bone marrow presented largely by pictures. However, there are also brief but adequate descriptions of the various diseases of the blood.

The book contains 285 illustrations of which 42 are in color. Practically all of the illustrations are photomicrographs, and marrow tissue sections are given the same prominence as blood and bone marrow films. Many of the legends include clinical features of the individual case. The coloring of the blood cells is excellent. However, the combination of May-Gruenwald and Giemsa stain used by the author does not demonstrate the fine nuclear detail shown by Wright's stain. The many large micro fields at high magnification afford a good standard for comparison. The effect of physical and chemical agents and of infection on the blood and bone marrow are thoroughly described and illustrated. The last chapter deals with the technique of bone marrow examination.

This atlas can be highly recommended to all those interested in the field of hematology. A study of its contents is worth the time of every physician.

HOWARD L. ALT.

ACCORDING to the opening statement in the author's preface to *Diseases of the Heart*[2] "This book endeavors to provide a comprehensive and integrated exposition of the diseases of the heart." In the reviewer's opinion, this premise is amply fulfilled.

The material of the book is well organized, with an excellent bibliography, and there is a splendid index. The publisher has done a good job with the illustrations and the printing.

The chapters on congestive heart failure deserve special commendation, particularly the discussion of digitalis therapy and mercurial diuretics. Recent advances in the fields of congenital heart disease and of subacute bacterial endocarditis are also given exceptional treatment.

This book deserves a place in any physician's library.

CHAUNCEY C. MAHER.

THE second edition of *Skin Grafting*[3] presents a timely review of the problem of treating the burned patient in addition to presenting some of the current developments in the field of reparative surgery where defects of the body surface due to trauma need resurfacing by split thickness grafts, full thickness grafts, or pedicle flaps.

The methods used represent the experiences of the authors in one of the largest reconstructive clinics in the country. The descriptions of their technique are so concise that even the surgeon who handles a burn only occasionally could discharge his obligation to his patient by following the text.

Profusely illustrated (239 illustrations), it permits the reader to follow the text with excellent photographs and illustrations.

The value of whole blood transfusions in the early care of burns and of the restoration of blood volume in the "chronic burn" has been clearly emphasized. Greater emphasis has also been placed on the condemnation of the tannic acid treatment of burns in favor of the use of occlusive pressure dressings following meticulous cleansing and débridement.

The chapter on "Surgical Repair of Radiation Injuries" which has been added to the second edition is in itself a most valuable monograph and the chapter entitled "Skin Grafting in Military Plastic Surgery" indicates the quality of the work performed by the senior author in the military service.

All who are interested in reparative surgery should find it a most useful reference book.

W. H. STEFFENSEN.

THE publication of Professor Glocker's *Roentgen- und Radiumphysik fuer Mediziner*[4] is timely, in keeping with the upsurge of interest in all phases of physics relating to radiation. At this time the scientific world is devoting special attention to the new knowledge of the atom and its application to medicine, both clinical and research. The author has produced a very practical manual of radiation physics

[1] AN ATLAS OF THE BLOOD AND BONE MARROW. By R. Philip Custer, M.D. Philadelphia and London: W. B. Saunders Co., 1949.

[2] DISEASES OF THE HEART. By Charles K. Friedberg, M.D. Philadelphia and London: W. B. Saunders Co., 1949.

[3] SKIN GRAFTING; TRAUMATIC AND OTHER SURFACE DEFECTS, INCLUDING APPLICATION OF PEDICLE FLAPS. By James Barrett Brown, M.D., and Frank McDowell, M.D. 2d ed. Philadelphia, London, and Montreal: J. B. Lippincott Co., 1949.

[4] ROENTGEN- UND RADIUMPHYSIK FUER MEDIZINER. By Prof. Richard Glocker. Stuttgart: Georg Thieme, 1949 (New York: Grune & Stratton, Inc., Agents for U. S. A.).

for physicians. A valuable contribution is the final section which includes an extensive bibliography, carefully classified under 12 headings. Many publications in English and French are included in this bibliography. JAMES T. CASE.

THE small book entitled *Die kuenstliche Schwangerschaftsunterbrechung, Indikationen und Methoden*,[1] prepared by Hans Naujoks, was originally written by Georg Winter who prepared two editions, one in 1925 and the other in 1932. The book deals with the indications for artificial interruption of pregnancy. The first and largest portion of the book pertains to medical indications for therapeutic abortion. A large number of indications are listed including the pregnancy toxemias, anomalies of the pelvic organ, disturbances of pregnancy itself, diseases of the internal organs including the respiratory tract, the cardiovascular system, the renal apparatus, blood diseases, and disturbances of internal secretion. There is also a large section devoted to psychiatric and neurologic diseases which the author believes may be used as indications for the interruption of a gestation. In this group, the author includes psychoses, epilepsy, chorea, and diseases of the brain, of the spinal cord, and of the peripheral nerves. Other medical indications are afflictions of the eye and ear. The author also lists surgical complications such as cancer, hernia, ileus, appendicitis, cholecystitis, and diseases of the bones and joints as possible indications for therapeutic abortion.

Among the nonmedical indications, the author discusses the eugenic, the social and the economic aspects. The last section is devoted to methods of interrupting pregnancy.

The reviewer by no means agrees with all the indications listed for therapeutic abortion.

The fact that this book has appeared in three editions proves that it has been popular in Germany. Those who can read German will find it interesting.

J. P. GREENHILL.

THE textbook *Injuries of the Brain and Spinal Cord and Their Coverings*[2] is the composite work of 28 recognized authorities. Its scope is inclusive and it embraces all aspects of trauma to the brain and spinal cord. The book suffers little, if at all, from the redundancy and repetitition which so often blights a work contributed to by several authors. In addition to the subjects usually discussed in a textbook dealing with trauma to the central nervous system, this book presents comprehensive treatment of the posttraumatic convulsive and allied states, neuroses and psychotic states following head injury, the relation of trauma to other organic diseases of the brain and spinal cord, birth injuries, and a valuable chapter on the medicolegal aspects of trauma to the brain and spinal cord.

The material presented is up to date and inclusive. Because of the frequency of injuries of the skull, brain, and spinal cord, they have assumed an important place in the practice of neurology, psychiatry, and neurosurgery. The consequences of such trauma also claim the attention of physicians engaged in the practice of industrial medicine, of officials of insurance companies, referees of compensation commissions, attorneys, and judges. To this group, the third edition is highly recommended.

H. J. SVIEN.

THE 517 page volume *Problems of the Human Brain. Selective Partial Ablation of the Frontal Cortex: a Correlative Study of its Effects on Human Psychotic Subjects*[3] constitutes the official group report of the Columbia-Greystone Project conducted at the New Jersey State Hospital at Greystone Park under the auspices of the Department of Neurology of Columbia University. It includes a large number of reports written by 43 contributors from the fields of neurology, psychiatry, psychology, medicine, neurosurgery, otolaryngology, anatomy, pathology, and statistics. It is an attempt to discover whether selective partial ablation of the frontal cortex (topectomy) yields results as satisfactory or better than those obtained by lobotomy in the treatment of psychoses. It presents the detailed neurological, psychological, clinical and laboratory studies of 48 patients of whom 24 were operated upon.

Section 1 of the report describes the method of selection of the patients in the age group 20 to 61 and suffering from various forms of schizophrenia, manic depressive psychosis, and involutional psychosis. The surgical procedure conducted by Lawrence Pool is outlined in detail with the help of operative photographs and diagrams. Prefrontal lobotomies were performed on another group of 8 patients, 6 of whom previously belonged to the control group of patients. A chapter written by Fred Mettler is devoted to the cytoarchitecture of the frontal lobes based on the histological study of the cortical areas which were resected. It was found that Brodmann's cytoarchitectural map was of practical value although it had no absolutely accurate anatomical basis.

In Section 2 the results of detailed laboratory data are presented and discussed. Glucose tolerance tests suggested that the granular cortex of the frontal lobes exerted an influence in carbohydrate metabolism. Increase in the production of combined and free acid in the stomach was also noticed following topectomy and lobotomy. No disturbances in gastrointestinal motility could be found following topectomy, but after lobotomy hastening of gastric and

[1] DIE KUENSTLICHE SCHWANGERSCHAFTSUNTERBRECHUNG, INDIKATIONEN UND METHODEN. By Prof. Dr. Hans Naujoks. Stuttgart: Ferdinand Enke Verlag, 1949.

[2] INJURIES OF THE BRAIN AND SPINAL CORD AND THEIR COVERINGS; NEURO-PSYCHIATRIC, SURGICAL, AND MEDICO-LEGAL ASPECTS. Edited by Samuel Brock. 3d ed. Baltimore: The Williams & Wilkins Co., 1949.

[3] PROBLEMS OF THE HUMAN BRAIN. SELECTIVE PARTIAL ABLATION OF THE FRONTAL CORTEX; A CORRELATIVE STUDY OF ITS EFFECTS ON HUMAN PSYCHOTIC SUBJECTS. By The Columbia-Greystone Associates. Fred A. Mettler, M.D., Ph.D., Editor. New York: Paul B. Hoeber, Inc., 1949.

intestinal motility was observed. No permanent changes could be found in the function of the visual, vestibular and auditory apparatus, and study of blood cells, blood chemistry, and blood pressure failed to disclose any definite permanent alterations following topectomy.

Section 3 contains detailed reports of psychologic investigations made before and after operation and of follow-up tests made one year later. No permanent alterations of intellectual function were found after topectomy. Ability to learn, retain material learned, ability to abstract and time judgment were not impaired. Some changes were found in word association tests but no other changes in mnemonic function could be obtained. No definite changes in personality trends could be found on examination of the Rorschach tests although there was a tendency toward a decrease of anxiety and ambition factors and an increase in inaccuracy. Bilaterial removal of Brodmann's areas 9, 10 and 46 resulted in some patients in a decrease of the anxiety and complaints, suggesting affective stabilization and loss of psychomotor tension.

Section 4 is devoted to psychiatric, neurologic and pathologic investigations and contains an abstract of the case histories of all patients. Psychiatric results compared favorably with those following other types of surgery in the treatment of psychoses. Improvement occurred more often among the younger patients and those whose illnesses were of shorter duration and who had favorable responses to shock therapy prior to operation. Regardless of the cortical area removed, a transient increase in abnormal behavior takes place in every patient. It seemed that removal of a specific region of cortex involving areas 9 and 10 resulted in clinical improvement, altering the affective responses of the patient. This change in affective behavior is essentially the same following prefrontal lobotomy, but the lobotomy patients show the tactless, carefree, irresponsible behavior with lack of initiative and absence of remorse that was characteristic of the topectomy patient who had too large an area of cortex removed. Patients with agitated depressions and agitated involutional paranoia, because of the affective component of their illness, have a very favorable prognosis. Only schizophrenics in whom there is an affect appropriate to ideation have a reasonable chance for improvement.

Neurologic examinations revealed a few interesting observations. Two patients in whom Broca's area was removed bilaterally did not have anarthria or motor aphasia. Removal of area 6 resulted in incontinence in every patient. None of the operatees showed evidence of ataxia, dysmetria or past-pointing as occasionally seen in frontal lobe tumors.

Pathological studies of the areas of cortex removed at operation showed remarkably few unspecific abnormalities. Histochemical methods such as the demonstration of alkaline and acid phosphatase and of ceroid pigment brought to light no deviations from control material.

Three separate summaries of findings in anatomy and physiology, psychology and psychiatry constitute Section 5.

This book is a monument to planned clinical and laboratory investigation and especially to successful co-operative research. It should serve as a basis for further investigative work and it delineates directions for future studies. It should be read and studied by psychiatrists and psychologists as well as the students of cerebral physiology. GEORGE PERRET.

THE monograph *Practical Aspects of Thyroid Disease*[1] which is written "to present the picture of diseases of the thyroid gland in such a way that medically trained readers may emerge with a better understanding of the aims of the surgeon, and surgically trained readers may better understand what the internists and radiologists are able to accomplish" probably accomplishes the stated objectives.

Nine of the 27 chapters are devoted to the surgical treatment of hyperthyroidism, i.e., preoperative management of hyperthyroidism, anesthesia for thyroidectomy, anatomy of the thyroid, technique of thyroidectomy, results of thyroidectomy and evaluation of technique, complications during thyroidectomy, postoperative care and postoperative complications, and recurrent hyperthyroidism. As one would expect, Dr. Crile has written these chapters well and interestingly. Surgeons and internists who are interested in the management of disease of the thyroid will profit by reading these chapters.

Five chapters are devoted to a discussion of cancer of the thyroid. The classification the author presents for malignant tumors of the thyroid is as follows: Carcinoma—(1) papillary carcinoma; (2) non-papillary carcinoma including (a) angio invasive adenoma, (b) adenocarcinoma, (c) undifferentiated carcinoma; (3) special types including (a) non-encapsulated sclerosing tumor, (b) squamous cell carcinoma, (c) metastatic carcinoma. Sarcoma—(1) lymphoma, and (2) spindle cell sarcoma. Dr. Crile and his associates have found this classification to be a practical one. The reviewer's only quarrel with such a classification is the same that he has with most published systems of classification. Too often these tumors are mixed and contain components of several of the nonpapillary tumors along with the papillary components. The spindle cell tumor has been observed by the reviewer when grown in the anterior chamber of a guinea pig's eye to present epithelial cells in an alveolar fashion. This observation is hardly consistent with the classification of sarcoma. Finally one would prefer a classification system which would be more descriptive than those now available. The present studies on the function of such tumors and their correlation with structure may ultimately not only make such descriptive classification possible but mandatory.

In discussing the incidence of carcinoma of the

[1] PRACTICAL ASPECTS OF THYROID DISEASE. By George Crile, Jr., M.D., F.A.C.S. Philadelphia and London: W. B. Saunders Co., 1949.

thyroid, Crile expresses a healthy skepticism of the high figures reported by several clinics. Of the cases that he reports, however, 10.9 per cent of 274 nontoxic nodular goiters and 24.5 per cent of 98 solitary nodules were malignant. He states, however, that of those goiters which were malignant the diagnosis of cancer was made preoperatively in 90 per cent. He wisely suggests that nodular goiters be treated on an individual rather than on a statistical basis.

In discussing papillary carcinoma of the thyroid he confesses his conversion to the thesis that these tumors are primary cancers arising in the thyroid which metastasize to the cervical lymph nodes. In discussing the treatment of this type of cancer he argues against block dissection of the neck. His arguments are that "the lateral cervical nodules rarely invade muscle or blood vessels." Due to the slow rate at which this tumor progresses, it will probably take many years before one can say who is right, those who adhere to Crile's theory or those who advocate radical block dissection in all patients having papillary carcinoma of the thyroid.

The chapters on congenital abnormalities, thyroiditis, and intrathoracic goiter, prevention and treatment of endemic goiter are presented well and interestingly.

However, the chapters on physiology, pathology, clinical and pathologic aspects of hyperthyroidism, diagnosis of hyperthyroidism, antithyroid drugs, and roentgenotherapy and radioactive iodine in the treatment of hyperthyroidism leave much to be desired.

The reviewer adheres to the philosophy that even a monograph on the "practical aspects" of thyroid disease should present an adequate and lucid discussion of physiology, pathology, and the pathologic physiology of the thyroid. Unfortunately such a presentation is lacking in this monograph. After careful study of these sections of the book, one is left with the impression that the author is apologizing for presenting any discussion of these important facets of such a book. His section on pathology would add to the "practical aspects" of the book if illustrated with examples of thyroid pathology.

Throughout the monograph one is impressed by the inadequate bibliography. Indeed in several instances there are misquoted references. For example, he states on page 5 "—MacKenzie, MacKenzie and McCollum had found that rape seed diets induced goiters in rats—." Actually these investigators reported that rats receiving sulfaquanidine developed goiters. In a subsequent paper they reported that other sulfonamides had goitrogenic properties. The goitrogenic properties of rape seed were described in 1941 by Kennedy, Purves, and Griesbach.

It is surprising to the reviewer that a surgeon of Crile's experience should say as he does on page 52, "there is little or no clinical difference between hyperthyroidism associated with diffuse and with nodular goiters since the response of both types to iodine and the antithyroid drugs is favorable." It is quite possible, however, that this statement represents an error which slipped the red pencil of the proof reader, since on page 92 he writes "There is reason to believe that propyl thiouracil is not effective in controlling hyperthyroidism associated with nodular goiters."

In discussing the "technique of treatment with I^{131}," Crile describes an empiric method of administering radio iodine without previous tracer studies. The reviewer agrees that this is a simple and relatively inexpensive method of treating hyperthyroidism. However, such a method of administering this isotope may be associated with certain risks and hazards. It certainly is not an instructive method for using this isotope in the study of thyroid disease.

Notwithstanding the fact that the reviewer has been critical of certain sections of this monograph, he does find it to be an interesting and well illustrated presentation of one practicing surgeon's philosophy of thyroid disease. Dr. Crile is to be congratulated on his honest presentation of his own experiences and philosophies in the treatment of these diseases.

RULON W. RAWSON.

THE author's thorough understanding of his subject allows him to present it in clear, concise and logical form. The text *Bone and Joint Radiology*[1] is divided under the general headings of congenital, traumatic, neoplastic, infectious, endocrine, and changes in blood elements. The groundwork for a thorough and ready understanding of these well written and documented chapters is laid in 3 excellently written sections devoted to the histology, anatomy, and physiology of bone. The text constitutes a comprehensive discussion not only of the disease processes but their relation to various parts of the skeleton.

The volume is well illustrated, with self-explanatory roentgenograms, well captioned. Diagrammatic sketches allow for ready reference and quick assimilation of the text material. An extensive bibliography offers good access of the text.

JAMES T. CASE.

THE new book *Modern Practice in Anaesthesia 1949*[2] has been much changed in character from the compendium with a similar title published in the *Practitioners' Handbook* series. If it is to be considered as a successor to the latter, it must be judged to have failed in its object. The original work was brief, concise and as dogmatic as necessary in laying down the fundamental principles of anesthesia, together with practical aspects, for general practitioners who wished to undertake administration of an occasional anesthetic. This new compendium is by comparison, cumbersome and somewhat repetitive. It is unfortunate that the editor, in picking his con-

[1]BONE AND JOINT RADIOLOGY. By Emerik Markovits, M.D. New York: The Macmillan Co., 1949.

[2]MODERN PRACTICE IN ANAESTHESIA 1949. Edited by Frankis T. Evans, M.B., B.S., F.F.A.R.C.S., D.A. New York: Paul B. Hoeber, Inc., 1949.

tributors, should have chosen to include only those practicing within the London area. The book, therefore, cannot be considered as representative of Great Britain as a whole.

While it is agreed that knowledge of the basic sciences forms a fundamental part of the successful practice of anesthesia, it is doubtful if that knowledge can be successfully compressed into 3 or 4 chapters of a book endeavoring to cover all aspects of the specialty. This is expecially true since good textbooks are available to provide the requisite basic knowledge, though clear restatement of these fundamentals, stripped of minutiae, may be advantageous. Errors have crept in that one hopes will be corrected in future editions.

In other chapters of the book, new ideas are propounded, which, while they may not be generally accepted, will provide an interesting basis for discussion; for example, Dr. Morris has simplified the description of the stages of anesthesia, adapting them somewhat to present day concepts. The chapters on preparation of the patient and on blood transfusion and fluid replacement, are worthy of commendation with reservations in regard to discussion of the rhesus factor.

This book is recommended as an interesting addition for the library of the professional anesthesiologist but is not recommended as a textbook for beginners or for the occasional anesthetist.

RANALD J. M. STEVEN AND RALPH M. TOVELL.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

AETIOS OF AMIDA; THE GYNECOLOGY AND OBSTETRICS OF THE VITH CENTURY, A.D. Translated from the Latin edition of Cornarius, 1542 and fully annotated. By James V. Ricci, A.B., M.D. Philadelphia, Toronto: The Blakiston Co., 1950.

LA CHIRURGIE A DEUX ÉQUIPES DANS LE TRAITEMENT DES CANCERS PELVIENS. By A. Ameline, J. Huguier, P. Moyse, and Y. Chatain. Paris: Librairie Arnette, 1950.

ANXIETY IN PREGNANCY AND CHILDBIRTH. By Henriette R. Klein, M.D., Howard W. Potter, M.D., and Ruth B. Dyk, M.S. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 1950.

PERSONALITY IN PEPTIC ULCER. By A. J. Sullivan, M.D., and Thomas E. McKell, M.D. Springfield, Ill.: Charles C Thomas, 1950.

SUPÉRVOLTAGE ROENTGENTHERAPY. By Franz Buschke, M.D., Simeon T. Cantril, M.D., and Herbert M. Parker, M.Sc. Springfield, Ill.: Charles C Thomas, 1950.

THE MERCK MANUAL OF DIAGNOSIS AND THERAPY; A SOURCE OF READY REFERENCE FOR THE PHYSICIAN. 8th ed. Rahway, New Jersey: Merck & Co., Inc., 1950.

ORAL AND FACIAL CANCER. By Bernard G. Sarnat, M.D., F.A.C.S., and Isaac Schour, D.D.S., Ph.D., ScD. With a Foreword by Andrew C. Ivy, Ph.D., M.D., D.Sc. Chicago: The Year Book Publishers, 1950.

CLINICAL USES OF INTRAVENOUS PROCAINE. By David J. Graubard, M.D., and Milton C. Peterson, M.D. Springfield, Ill.: Charles C Thomas, 1950.

PRIMARY CARCINOMA OF THE VAGINA. By Robert G. Livingstone, M.D. Springfield, Ill.: Charles C Thomas, 1950.

MODERN TRENDS IN ORTHOPAEDICS. Edited by Sir Harry Platt, M.D., M.S., F.R.C.S. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 1950.

PATHOLOGY IN GENERAL SURGERY. By Paul W. Schafer, M.D., Chicago: The University of Chicago Press; London: Cambridge University Press; Toronto: W. J. Gage & Co., 1950.

THE GENEAOLOGY OF GYNAECOLOGY; HISTORY OF THE DEVELOPMENT OF GYNAECOLOGY THROUGHOUT THE AGES 2,000 B.C.—1,800 A.D. WITH EXCERPTS FROM THE MANY AUTHORS WHO HAVE CONTRIBUTED TO THE VARIOUS PHASES OF THE SUBJECT. By James V. Ricci, A.B., M.D. 2d rev. enl. ed. Philadelphia, Toronto: The Blakiston Co., 1950.

CHEMOTHERAPIE DER TUBERKULOSE MIT DEN THIOSEMIKARBAZONEN. By Prof. Dr. G. Domagk. Stuttgart: George Thieme; New York: Grune & Stratton, Inc., 1950.

CONTRIBUIÇÃO PARA A SEMIOLOGIA FUNCTIONAL DA SECREÇÃO CLORÍDRICA E DA REGULAÇÃO DA ACIDEZ GÁSTRICA. By Jose Ramos de Oliveira Junior. São Paulo: University of São Paulo, 1949.

THE FIRST ANESTHETIC; THE STORY OF CRAWFORD LONG. By Frank Kells Boland, M.D. Athens: University of Georgia Press, 1950.

HAVING A BABY. By Alan F. Guttmacher, M.D. 2d rev. ed. New York: The New American Library, 1950.

ATLAS OF HUMAN ANATOMY; DESCRIPTIVE AND REGIONAL. By M. W. Woerdeman, M.D., F.R.N.A.Sc. Vol. 2. Philadelphia, Toronto: The Blakiston Co., 1950.

THE CEREBRAL CORTEX OF MAN; A CLINICAL STUDY OF LOCALIZATION OF FUNCTION. By Wilder Penfield, C.M.G., M.D., B.Sc., and D.SC. (Oxon.), Hon.F.R.C.S. (Lond.), F.R.S., and Theodore Rasmussen, M.D. New York: The Macmillan Co., 1950.

COMBINED TEXTBOOK OF OBSTETRICS AND GYNAECOLOGY FOR STUDENTS AND PRACTITIONERS. Edited by Dugald Baird, B.Sc., M.D., D.P.H., F.R.C.O.G. 5th ed. Baltimore: The Williams & Wilkins Co., 1950.

LE PROBLÈME DU CANCER. By Prof. Dr. Frans Daels. Geneve: L'Effort Humain, 1950.

MATERNITY CARE IN TWO COUNTIES; GIBSON COUNTY, TENNESSEE, PIKE COUNTY, MISSISSIPPI, 1940–1941, 1943–1944. By Dr. Frank E. Whitacre, M.D., and Ellen Whiteman Jones, M.P.H. New York: The Commonwealth Fund, 1950.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

FREDERICK A. COLLER, Ann Arbor, *President*
HENRY W. CAVE, New York, *President-Elect*

PRELIMINARY PROGRAM FOR THE 36th CLINICAL CONGRESS—HOTEL STATLER, BOSTON OCTOBER 23 TO 27, 1950

ADVANCE registrations show that hotels and auditoriums will be taxed to capacity for the thirty-sixth Clinical Congress of the American College of Surgeons which will be held in Boston from October 23 to 27, 1950. The facilities, however, are excellent, and with the use of meeting rooms in Mechanics Hall, Symphony Hall, the New England Mutual Building, and the Statler and Copley-Plaza hotels, good accommodations are assured. The inconvenience of not having all meetings under one roof will be minimized by the fact that the buildings are within easy walking distance of one another.

The tentative assignment of sessions to the various buildings is as follows:

Mechanics Building:

General Assembly—Monday a.m.
Color Television—daily
Medical Motion Pictures—daily
Symposium on Sports Injuries—Tuesday a.m.
Clinico-pathological Conference—Wednesday a.m.
Symposium on Trauma—Thursday a.m.
Assembly of Initiates—Friday a.m.

Symphony Hall:

Convocation—Friday evening

New England Mutual Building:

Forums on Fundamental Surgical Problems—Thursday a.m. and p.m.
Panel on Plastic Surgery—Friday p.m.
Panel on Thoracic Surgery—Friday p.m.

Hotel Statler:

Forums on Fundamental Surgical Problems—Monday p.m., Tuesday and Wednesday a.m. and p.m., Friday a.m.
All hospital conferences
Presidential Meeting—Monday p.m.
General Surgery sessions—Tuesday and Wednesday evenings
Cancer Symposium—Wednesday p.m.
Graduate Training in Surgery Symposium—Thursday p.m.
Panel on Gynecology and Obstetrics—Friday p.m.
Panel on Urology—Friday p.m.

Copley-Plaza Hotel:

Sessions and medical motion pictures on Ophthalmology—Tuesday, Wednesday and Thursday afternoons and evenings
Sessions and medical motion pictures on Otorhinolaryngology—Tuesday, Wednesday and Thursday afternoons and evenings
General Surgery session—Thursday evening
Annual Meeting of Fellows—Thursday p.m.
Panel on Orthopedic Surgery—Friday p.m.

POSTGRADUATE COURSES

A new feature of the Boston Clinical Congress will be the holding of a series of five postgraduate courses on the following subjects:

Nutrition of the Surgical Patient
Vascular Diseases
Fractures of the Spine and Skull
Fractures of the Long Bones
Preoperative and Postoperative Care

Each course will consist of five half-day sessions and will be conducted in the forenoons at the Boston City Hospital, Massachusetts General Hospital, Massachusetts Memorial Hospital, Children's Hospital, and Peter Bent Brigham Hospital. Admission tickets will be arranged so that applicants may register for a complete course or for portions of any courses.

COLOR TELEVISION

Telecasts in color of operations taking place at the Massachusetts General Hospital will be shown in a room in the Mechanics Building every afternoon, Monday through Thursday, and every morning except Monday. Dr. Horatio Rogers of the hospital staff will be in charge of the television.

This demonstration is made possible by Smith, Kline & French Laboratories of Philadelphia. It was at their request that Columbia Broadcasting System, Inc., undertook to specially design and manufacture color television equipment for teaching surgery and medicine. This equipment, the first of its kind to date, is owned by the Laboratories and is being demonstrated by them throughout the country as a contribution to medical teaching. This will be the second demonstration at a Clinical Congress, the first having been in Chicago in October, 1949. Previously, at the Congresses in Los Angeles in 1948 and in New York in 1947, the television was in black and white. The Los Angeles showing was sponsored by the *Los Angeles Times* and the New York showing which was the first use of television at a national medical meeting, was made possible by a grant from the Johnson & Johnson Research Foundation.

HOSPITAL CLINICS

Under the leadership of the Committee on Arrangements, and the hospital representatives, a program of operative and nonoperative clinics is being arranged in 25 hospitals, as a major feature of the Clinical Congress. The schedules of clinics, which will cover general surgery, obstetrics and gynecology, fractures and other trauma, neurosurgery, orthopedic, thoracic, and genitourinary surgery, and ophthalmology and otorhinolaryngology, will be published in a *Daily Clinical Bulletin* which will be issued each day during the Clinical Congress. The clinic schedules will also be posted on bulletin boards.

PRESIDENTIAL MEETING AND CONVOCATION

Dr. Frederick A. Coller of Ann Arbor, the retiring President, will deliver the Presidential Address at the Presidential Meeting on Monday evening. His subject will be "For The Benefit of the Patient." At the same session Dr. Henry W. Cave of New York will be installed as President, and Dr. Warren H. Cole of Chicago and Dr. G. Gavin Miller of Montreal as First and Second Vice Presidents respectively. The fifth Martin Memorial Lecture will be delivered by Mr. Geoffrey Jefferson, C.B.E., F.R.C.S. (Eng.). His subject will be "The Balance of Life and Death in Intracranial Lesions."

The annual Convocation which includes formal initiation ceremonies for the new Fellows will take place on Friday evening, October 27, in Symphony Hall. The Fellowship Address will be given by Dr. Paul R. Hawley, Director of the College. His subject will be "Quo Vadimus?"

MEETINGS OF THE BOARD OF GOVERNORS AND FELLOWS

The Board of Governors of the College will convene with luncheon on Monday and will meet from 12:45 to 5:00 p.m. Any unfinished business will be discussed at a session on Wednesday morning. There will be an adjourned meeting at 3:30 p.m. on Thursday.

The Governors will act as a clearing house for the Board of Regents on general assigned subjects and on local problems. They are being apprised of the actions taken by the Board of Regents and will aid in interpreting them to the Fellows.

The Annual Meeting of Fellows will be held on Thursday afternoon at 3:45. The agenda follow:

Election of Officers and Governors of the College
Report of the Treasurer
Report of the Cancer Committee
Report of the Committee on Trauma
Report of the Committee on Graduate Training in Surgery
Report of the Committee on Medical Motion Pictures
Report of the Director on the College Program
General Discussion (30 minutes)

COMMITTEE MEETINGS

There will be a meeting of State and Provincial Counseling Committees (formerly State and Provincial Executive Committees), Credential Committees, Committees on Applicants and Judiciary Committees, on Wednesday from 10:00 a.m. until noon at the Copley-Plaza Hotel. Dr. Paul R. Hawley, Director of the College, will discuss the role of these committees in elevating the prestige of the College and Dr. H. Prather Saunders, Associate Director, will describe consideration of applicants for the Junior and Senior Candidate Groups and for Fellowship.

COMMITTEE ON ARRANGEMENTS

The Boston Committee on General Arrangements for the Clinical Congress is composed of the following Fellows:

*Thomas H. Lanman, *Chairman*
*Donald Munro, *Vice-Chairman*
*Orvar Swenson, *Secretary*
*Arthur W. Allen, *Chairman*, Board of Regents

Edwin W. Cave	Joe Vincent Meigs
Edward D. Churchill	Charles G. Mixter
Fletcher H. Colby	Francis D. Moore
Edwin B. Dunphy	William R. Morrison
*J. Englebert Dunphy	*Langdon Parsons
Henry H. Faxon	Walter G. Phippen
Robert E. Gross	Duncan E. Reid
Frank H. Lahey	LeRoy A. Schall
Charles C. Lund	Reginald H. Smithwick
Leland S. McKittrick	Grantley W. Taylor
Henry C. Marble	*C. Stuart Welch

*Executive Committee

Boston was host to the Clinical Congresses of 1915, 1922, 1928, 1934, and 1941. Notable contributions to surgical and medical knowledge were made at these meetings. Those who attend in 1950 may anticipate a program of broad scope and interest, for the surgeons of Boston have complete facilities at their command in the three medical schools and more than thirty approved hospitals in Boston and vicinity.

GENERAL, PROGRAM, AND PUBLIC RELATIONS COMMITTEES

The Clinical Congress General Committee consists of Dr. Paul R. Hawley, Chairman, Eleanor K. Grimm, Secretary, Dr. Charles F. Branch, Laura G. Jackson, Dr. George H. Miller, Edward G. Sandrok, Dr. H. Prather Saunders, and James S. Shannon.

The Clinical Congress Committee on Programs consists of Dr. Frederick A. Coller, Chairman, and Doctors Henry W. Cave, Evarts A. Graham, and Alton Ochsner. Programs for the specialties are being arranged in co-operation with the Advisory Council of the College on ophthalmology, otorhinolaryngology, neurological surgery, obstetrics and gynecology, orthopedic surgery, thoracic surgery, and urology.

The Advisory Committee on Programs consists of Dr. George H. Miller, Chairman, and Doctors Warren H. Cole, Sumner L. Koch, Michael L. Mason, Charles B. Puestow, Paul R. Hawley, H. Prather Saunders, Charles F. Branch, and Malcolm T. MacEachern.

The Public Relations Committee consists of Dr. Charles B. Puestow, Chairman, members of administrative staff, American College of Surgeons, and members of the local committee on publicity, of which Dr. Charles C. Lund is Chairman.

EVENING SCIENTIFIC SESSIONS

Eminent surgeons and specialists, recognized as authorities in their fields, will address the scientific meetings which will be held on Tuesday, Wednesday, and Thursday evenings. The preliminary program for the general surgery sessions follows:

Tuesday, October 24

The Concept of the General-Adaptation-Syndrome as Applied to Surgical Problems (with Special Emphasis upon Cortisone and ACTH). HANS SELYE, Montreal.
Biophysics in Surgery. AMBROSE STORCK, New Orleans.
The Principles Involved in the Clinical Use of Streptokinase-Streptodornase. WILLIAM S. TILLETT, New York.

Wednesday, October 25

Fracture Oration. (Selected by Committee on Trauma).
Intravenous Fat Feeding. FREDERICK J. STARE, Boston.
The Neurological Complications of Spinal Anesthesia. R. D. DRIPPS, Philadelphia.

Thursday, October 26

Lobotomy Versus Other Operations for the Relief of Pain. JAMES C. WHITE, Boston.
The Etiology and Treatment of Hirschsprung's Disease. ORVAR SWENSON, Boston.
Late Surgical Complications Following Irradiation of Pelvic Viscera. WILLIAM CRAWFORD WHITE, New York.

On Tuesday and Thursday evenings, there will be separate sessions for Ophthalmology and for Otorhinolaryngology. The Wednesday evening meeting will be a joint ophthalmology and otorhinolaryngology session with the New England Otolaryngological Society participating. A preliminary outline of the programs follows:

Tuesday, October 24, Ophthalmology

Ocular Effects of the Atomic Bomb in Japan
Evaluation of Retinal Vascular Diseases
Treatment of Pigmented Tumors of the Eye and Adnexa

Tuesday, October 24, Otorhinolaryngology

Modern Bacteriology as an Aid to the Otolaryngologist
The Influence of Fundamental Concepts in Allergy upon Specific Problems in Otolaryngology
The Present Status of the Relationship of Tonsillectomy to Poliomyelitis

Wednesday, October 25
Joint Session

Antibiotics Today. CHESTER S. KEEFER, Boston.
Ophthalmological Applications of the Newer Antibiotics. IRVING H. LEOPOLD, Philadelphia.
Use of Antibiotics in Otolaryngology. FRANCIS W. DAVISON, Danville, Pennsylvania.

Thursday, October 26, Ophthalmology

Glaucoma after Cataract Extraction
Present Trends of Surgery of the Oblique Muscles
End Results of Integrated Implants in the Orbit

Thursday, October 26, Otorhinolaryngology

Symposium on Tumors of the Nose and Sinuses:
Symptomatology
X-ray Diagnosis
Preparation and Care of the Mouth of the Patient Receiving X-ray Therapy about the Head and Neck
Treatment by a Combination of Surgery and Radiation

AFTERNOON PANEL DISCUSSIONS, GENERAL SURGERY

General surgery panel discussions will be held Monday through Thursday afternoons from 1:30 to 3:00 o'clock, and Monday through Wednesday afternoons from 3:30 to 5:00 o'clock. A preliminary outline follows:

Monday

1:30–3:00. Transthoracic Approach to Subdiaphragmatic Lesions. Moderator: B. NOLAND CARTER, Cincinnati.

3:30–5:00. Cancer of the Uterus. Moderator: JOHN C. BURCH, Nashville.

Tuesday

1:30–3:00. Complemental Combinations in Anesthesia. Moderator: WESLEY BOURNE, Montreal.
3:30–5:00. Reconstructive Surgery of the Hand. Moderator: HENRY C. MARBLE, Boston.

Wednesday

1:30–3:00. Surgical Treatment of Congenital Anomalies of the Digestive Tract. Moderator: LAWRENCE CHAFFIN, Los Angeles.
3:00–5:00. Pitfalls in Surgery of the Gallbladder and Biliary Ducts. Moderator: WALTMAN WALTERS, Rochester, Minnesota.

Thursday

1:30–3:00. Acute, Nontraumatic Conditions in the Abdomen. Moderator: FRED W. RANKIN, Lexington, Kentucky.

AFTERNOON PANEL DISCUSSIONS, OPHTHALMOLOGY AND OTORHINOLARYNGOLOGY

Ophthalmology and otorhinolaryngology panel discussions will be held Tuesday, Wednesday, and Thursday afternoons, in accordance with the following outline:

Tuesday

1:30–3:00. Ophthalmology: Chiasmal Syndrome
3:30–5:00. Otorhinolaryngology: The Pre-School Deaf Child

Wednesday

1:30–3:00. Ophthalmology: Diagnosis of Orbital Tumors
3:00–5:00. Otorhinolaryngology: What We Have Learned about Fenestration for Otosclerosis

Thursday

1:30–3:00. Ophthalmology: Selection of Operative Technic in Retinal Separation
3:30–5:00. Otorhinolaryngology: The Management of the Vertiginous Patient

AFTERNOON PANEL DISCUSSIONS, SURGICAL SPECIALTIES

Friday afternoon will be devoted to panel discussion sessions for six special fields of surgery. A preliminary outline of the programs follows:

Urology—Moderator, THOMAS D. MOORE, Memphis.
1:30–3:00. Injuries of the Ureter
3:15–4:45. Congenital Anomalies of the Lower Urinary Tract

Plastic Surgery—Moderator, JAMES BARRETT BROWN, St. Louis.
1:30–3:00. Plastic Surgical Repair of Radiation Lesions
3:15–4:45. Military Plastic Surgery

Neurological Surgery—
1:30–3:00. Moderator, BRONSON RAY, New York. Surgical Relief of Intractable Pain
3:15–4:45. Moderator, JOHN E. SCARFF, New York. Evaluation of the Results of Surgical Procedures Undertaken for the Relief of Psychoses

Thoracic Surgery—
1:30–3:00. Moderator, HERBERT C. MAIER, New York. Postoperative Pulmonary Complications
3:15–4:45. Moderator, FRANK B. BERRY, New York. Trauma of the Chest and Upper Abdomen

Gynecology and Obstetrics—Moderator, FREDERICK H. FALLS, Chicago.
1:30–3:00. Indications for Abdominal Total Hysterectomy for Nonmalignant Uterine Pathology
3:45–5:45. The Management of Urinary Incontinence in Women

Orthopedic Surgery—Moderator, G. EDMUND HAGGART, Boston.
1:30–3:00. The Management of Fractures and Dislocations of the Dorsal and Lumbar Spine
3:15–5:45. Fractures of the Elbow Region in Children

FORUM ON FUNDAMENTAL SURGICAL PROBLEMS

The Forum on Fundamental Surgical Problems at the 1950 Clinical Congress will again give special opportunity for the presentation of the newest discoveries resulting from research, particularly by the younger surgeons. Brief reports of original clinical and experimental observations relating to surgery in its broadest sense, including the surgical specialties, will be given. It is expected this year to have a few of the Forum sessions devoted to reports of research on a single surgical specialty. It is noteworthy that the Forum was first introduced in 1941 at the Boston Clinical Congress.

SYMPOSIA ON CANCER, TRAUMA, AND GRADUATE TRAINING IN SURGERY

Because of the widespread interest in these special fields, a Symposium on Trauma is being arranged for Thursday morning, and a Symposium on Cancer for Wednesday afternoon. There will be a Symposium on Sports Injuries on Tuesday morning. A Symposium on Graduate Training in Surgery is being planned for Thursday afternoon.

MEDICAL MOTION PICTURE PROGRAM

The Medical Motion Picture Committee is now choosing films which are to be shown at the Clinical Congress. Films that have been recently produced should be forwarded to the College for immediate review as it is the policy to include in the Clinical Congress program only those films which were submitted in time to obtain approval by the Committee on Medical Motion Pictures.

HOSPITAL CONFERENCES

The twenty-ninth Hospital Standardization Conference will convene during the Clinical Congress. Hospital administrators, trustees, members of medical staffs, nurses, technicians, dietitians, and heads of the various hospital departments and their personnel are invited to participate.

EXHIBITS

Mechanics Hall will house the extensive exhibit of medical and hospital supplies and equipment, television and medical motion picture showings, registration for surgeons and hospital representatives, and a few of the sessions. Leading manufacturers of surgical equipment and instruments, sutures, dressings, pharmaceuticals, and supplies of all kinds, and publishers of medical books will be represented in the exhibition.

HOSPITALS AND HOSPITAL REPRESENTATIVES

The hospitals which will arrange clinics for the 1950 Clinical Congress, and the names of the hospital representatives, follow:

Beth Israel Hospital—DR. HOWARD A. FRANK
*Boston City Hospital—DR. J. EDWARD FLYNN
Boston Lying-In Hospital—DR. PAUL GUSTAFSON
Carney HOSPITAL—DR. JOHN J. TODD
Chelsea Naval Hospital—DR. HENRY W. HUDSON
Children's Medical Center—DR. WILLIAM A. ELLISTON
Cushing Veterans Administration Hospital—DR. HENRY FAXON
Faulkner Hospital—DR. MARSHALL K. BARTLETT
Free Hospital for Women—DR. CHRISTOPHER J. DUNCAN
Malden Hospital—DR. CLEMENT LYNCH
Massachusetts Eye and Ear Infirmary—Ophthalmology—DR. HENRY A. MOSHER
Massachusetts Eye and Ear Infirmary—Otorhinolaryngology—DR. FRANCIS L. WEILLE
Massachusetts General Hospital—DR. HOWARD ULFELDER; Television chairman—DR. HORATIO ROGERS
Massachusetts Memorial Hospital—DR. GEORGE WHITELAW
Mount Auburn Hospital, Cambridge—DR. JOSEPH TARTAKOFF
New England Baptist Hospital—DR. HERBERT D. ADAMS
New England Center Hospital—DR. WYLAND LEADBETTER
New England Deaconess Hospital—DR. HERBERT D. ADAMS
New England Deaconess Hospital—Palmer Memorial Unit—DR. CLIFFORD FRANSEEN
New England Hospital for Women and Children—DR. FELICIA BANAS
Newton-Wellesley Hospital, Newton Lower Falls—DR. RICHARD I. SMITH
Peter Bent Brigham Hospital—DR. THOMAS B. QUIGLEY
Pondville Hospital, Walpole—DR. RICHARD WALLACE
Robert Breck Brigham Hospital—DR. THEODORE A. POTTER
St. Elizabeth's Hospital—DR. JOHN SPELLMAN
Veterans Administration Hospital—West Roxbury—DR. FREDERICK ROSS

POST CLINICAL CONGRESS COURSE

A course on Treatment of Fractures and Other Conditions will be held from October 30 to November 4, the week following the Clinical Congress, under the direction of Dr. Edwin F. Cave and associates of Massachusetts General Hospital. This course will deal primarily with the treatment of fractures, but the management of many other traumatic conditions will be presented. Attendance is limited to 100 students. Application should be made to the Assistant Dean, Courses for Graduates, Harvard Medical School, Boston.

*Through an oversight, Boston City Hospital was omitted in earlier issues of SURGERY, GYNECOLOGY AND OBSTETRICS.

ADVANCE REGISTRATION

Surgeons who wish to attend the Clinical Congress should register in advance. Advance registration will greatly expedite the procedure of registering. No registration fee will be charged Fellows whose dues are paid to December 31, 1949. For endorsed Junior and Senior Candidates, the fee will be $5.00. Non-Fellows who after individual consideration are permitted to register, will pay a fee of $10.00. No registration fee will be required of initiates of the class of 1950.

HOTEL RESERVATIONS

It is desirable to make hotel reservations as early as possible. In making these, communications should be addressed to the Convention Bureau of the Boston Chamber of Commerce, 80 Federal Street, Boston 10. It is important that you state you will be attending the Clinical Congress of the American College of Surgeons. All hotel reservations, both for surgeons and hospital representatives, are to clear through the Convention Bureau. No correspondence should be sent directly to the hotels. A form for reservations was enclosed in a letter to Fellows. Choice of hotels may be designated.

In addition to the headquarters hotels, the Statler and Copley-Plaza, there are a number of first-class hotels within a short distance of the Clinical Congress headquarters. The following hotels are recommended:

	Minimum Rate with Bath	
	Single	Double
Bellevue	$4.00	$ 6.00
Bradford	5.00	7.00
Copley-Plaza	5.00	7.70
Kenmore	5.00	9.00
Manger	4.00	5.50
New Ocean House, Swampscott	6.00	8.00
Parker House	4.50	7.00
Somerset	6.00	10.00
Statler	5.00	8.75
Touraine	4.50	7.00